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THE UNIVERSITY OF ALBERTA

THE CLINICAL EFFICACY AND SAFETY OF DIFLUNISAL IN SHORT TERM TREATMENT OF PAIN FOLLOWING ORAL SURGERY

by

© M. L. McCUE

A THESIS

SUBMITTED TO THE FACULTY OF GRADUATE STUDIES AND RESEARCH

IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE

OF MASTER OF SCIENCE

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FACULTY OF DENTISTRY

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FALL, 1978

THE UNIVERSITY OF ALBERTA

FACULTY OF GRADUATE STUDIES AND RESEARCH

The undersigned certify that they have read, and recommend to the Faculty of Graduate Studies and Research, for acceptance, a thesis entitled The Clinical Efficacy and Safety of Diflunisal in Short Term Treatment of Pain Following Oral Surgery submitted by Michael L. McCue in partial fulfillment of the requirements for the degree of Master of Science

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Date July 13, 1978

ABSTRACT

The Clinical Efficacy and Safety of Diflunisal
In Short Term Treatment of Pain Following
Oral Surgery

The object of the study was to compare the safety and efficacy of two salicylate derivatives, 2', 4'-difluoro-4 hydroxy- 3 biphenylcarboxylic acid (diflunisal) and acetylsalicylic acid in the short term (1.5 day) treatment of pain following surgical removal of impacted dental elements. Forty-two female and eighteen male subjects who were to undergo surgical removal of impacted teeth were selected to participate. The study was conducted single blind and the sixty patients were completely randomized within two treatment groups, one group received up to a total of 1250 mg diflunisal, the other received up to a total of 2500 mg acetylsalicylic acid. Administration of the medication was started at the onset of spontaneous pain following dental surgery.

Parameters of safety and efficacy were recorded by the investigator 24 hours following surgery and the results analyzed using the student "t" test and the chi square analysis of variance.

Diflunisal was found to be superior to acetylsalicylic acid in relieving pain following dental surgery. A sex difference was noted in that male subjects received more relief from both drugs than did the females, however the females received more relief from diflunisal than from acetylsalicylic acid. Male subjects reported no

such difference.

There were six adverse reaction experiences with diflunisal compared with two adverse reaction experiences with acetylsalicylic acid but this difference was not found to be statistically significant. In all cases the reactions were mild and of short duration.

ACKNOWLEDGEMENT

I wish to express my deepest gratitude to my wife Garnette whose assistance in preparing this thesis was invaluable.

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TABLE OF CONTENTS

Page

1.0 INTRODUCTION AND REVIEW OF THE LITERATURE..... 1

1.1 Pain 1

1.2 The Salicylates..... 1

1.3 Prostaglandins..... 2

1.4 Pain and Prostaglandins..... 3

1.5 Adverse Effects of Salicylates..... 4

1.6 Statement of the Problem..... 5

1.7 Discovery of Diflunisal..... 5

2.0 PURPOSE OF THE STUDY..... 9

3.0 MATERIALS AND METHOD OF INVESTIGATION..... 10

3.1 Diflunisal : Chemical and Pharmaceutical Data..... 10

3.2 Method of Investigation..... 11

4.0 RESULTS AND OBSERVATIONS..... 21

5.0 DISCUSSION..... 30

6.0 SUMMARY AND CONCLUSIONS..... 41

7.0 BIBLIOGRAPHY..... 43

8.0 APPENDIX..... 48

LIST OF TABLES

Table	Description	Page
1.	Diflunisal Versus A.S.A. for Pain Following Dental Surgery. Individual Patient Data Group I - Diflunisal	24
2.	Diflunisal Versus A.S.A. for Pain Following Dental Surgery. Individual Patient Data Group II - A.S.A.	25
3.	Diflunisal Versus A.S.A. for Pain Following Dental Surgery. Efficacy Summary	26
4.	Adverse Experiences	28
5.	Efficacy Ratings of Diflunisal Versus A.S.A.	31
6.	Pain Levels as Described by the Patient	33
7.	Degree of Surgical Trauma as Rated by the Oral Surgeon	34
8.	Efficacy Ratings by the Patient of Diflunisal Versus A.S.A. Grouped According to Sex	35
9.	Efficacy Ratings by the Investigator of Diflunisal Versus A.S.A. Grouped According to Sex	37
10.	Total Adverse Reactions Experienced by the Patients	39

LIST OF FIGURES

Figure		Page
1.	Schematic Diagram of Three Salicylate Derivatives	7
2.	Forms A and C of Data Sheet	13
3.	Form B of Data Sheet	17
4.	Bar Graph Illustrating the Age and Sex Distribution of Sixty Patients	22
Appendix Figures		
5-124	Data Forms A, B, and C for Each Patient.	49

1.0 INTRODUCTION

1.1 Pain

Pain is one of the most commonly experienced symptoms in dentistry and, as such, is a major concern to the dentist. To describe pain as "inevitable" or even "normal" is an attitude that should be condemned. A recent editorial by Locke (1976) in the British Medical Journal expressed concern that post operative pain has not aroused sufficient interest. It stated that "Both doctors and nurses are afraid of inducing addictions and, like many patients, have too complacently accepted pain as an inevitable consequence of surgery".

Post operative pain following dental procedures is an instance of this attitude that could also bear improvement.

Pain following many dental procedures, especially oral surgery, has been a very real concern to patients. Both narcotic and non-narcotic analgesics (usually the salicylate family) have been administered in order to relieve post operative pain. Although the narcotics possess greater analgesic potency than do the salicylates, their greater toxicity combined with more adverse reactions limit their application on a routine basis in dentistry.

1.2 The Salicylates

The term "salicylate" is used to describe a group of drugs which have in common the 2-hydroxybenzoate radical. The most important members in current clinical use are sodium salicylate and acetylsalicylic acid. The salicylate in chief use is acetylsalicylic acid, which is universally known as aspirin. They are drugs of great antiquity and their use in preparations from the leaves, bark and fruits of plants containing methyl salicylate and glycosides of salicyl alcohol

is as old as herbal therapy. In June of 1763 a paper by the Rev. Edward Stone (1763) was read at the Royal Society of London describing the "curative properties of an extract of willow bark (salix) on agues and intermitting disorders".

Despite the long history of the use of salicylates their mode of action has, until recently, remained virtually unexplained. Adams and Cobb (1958) suggested that uncoupling of oxidative phosphorylation could form the basis of the anti-inflammatory actions of aspirin-like drugs. Spector and Willoughby (1963) reported the anti-inflammatory properties of the salicylates were due to inhibition of the acitivity of the plasma kinin-forming enzymes thus preventing the release of bradykinin, a potent mediator of inflammation. Other possible interactions of salicylates with enzymes or chemical mediators of inflammation have been reviewed by Smith (1966) and Collier (1969). However, it was only during the last decade that researchers such as Ferreira et al (1971), Smith and Willis (1971) and Vane (1971) changed the entire concept of the mode of action of the salicylates by demonstrating that aspirin inhibits the biosynthesis of prostaglandins, substances involved in producing the pain of inflammation.

1.3 Prostaglandins

Prostaglandins are a group of pharmacologically active lipids with vasopressor and smooth muscle stimulating activity. They were discovered in accessory genital glands and human semen, in independent studies by von Euler (1934) and Goldblatt (1933). The name, prostaglandin, was first coined by von Euler (1935).

Bergstrom and Sjovall (1960) isolated two types, prostaglandin E_1 and prostaglandin $F_{1\alpha}$, in pure form and later Bergstrom (1963) identified

a large family of prostaglandins and determined their structures.

It is now known from studies by Bergstrom, Danielson and Samuellson (1964) and Van Dorp et al (1964) that prostaglandins are metabolic products derived from polyunsaturated fatty acids such as arachidonic acid and are found widely distributed in mammalian tissues and body fluids. Nakano (1973) found that prostaglandins have a wide variety of effects on each of the various systems of the body.

The importance of the presence of prostaglandins in the production of inflammation has been established by three broad but converging lines or research. First, Bergstrom (1959) found E type prostaglandins to have potent pro-inflammatory effects. This was confirmed in the following years by Kaley (1971), Collier (1972), Palmer (1973), Ferreira (1974) and Vane (1976). Vane (1976) working with a substance known to cause contractions in the rabbit aorta suggested that this substance may be an unstable cyclic peroxide intermediate in the biosynthesis of inflammation. Second, Willis (1969), Greaves (1971) and Higgs (1975) discovered that prostaglandins are released in several different types of inflammation. Third, Vane (1971), Smith (1971) and Ferreira (1972) reported that the non steroid anti-inflammatory drugs directly inhibit the biosynthesis of prostaglandins. Vane (1971) proposed that inhibition of enzymes necessary for prostaglandin biosynthesis was the basis for the mode of action of aspirin-like drugs.

1.4 Pain and Prostaglandins

Although Vane (1971) found that the aspirin-like drugs reduced inflammation and fever by inhibiting prostaglandin biosynthesis, there was no evidence for a link between the peripheral analgesic action of

the drug and inhibition of prostaglandin synthesis.

Several studies describing the pain producing activity of prostaglandins infused intravenously and injected intra-muscularly in man have now been reported by Collier (1972), Gillespie (1972), and Karim (1971). Collier and Schneider (1972) have shown that prostaglandin E_1 is the most powerful agent in producing writhing responses in mice.

Ferreira (1972, 1973) found that prostaglandins may cause overt pain, depending on their concentrations. However, in concentrations likely to be present in inflammatory reactions, they are thought of only to sensitize the pain receptors to the nociceptive action of bradykinin

The thesis has been developed by Vane (1971) Flower, Gryglewski et al (1972), and Ferreira and Vane (1974) that the concentrations of anti-inflammatory drugs in body fluids achieved after therapeutic dosages are adequate to inhibit prostaglandin biosynthesis. This has been substantiated by indirect and direct measurements in man. The first study by Smith and Willis (1971) demonstrated that oral ingestion of 600 mg aspirin or of 100 mg indomethacin by healthy human subjects almost completely prevented prostaglandin generation by platelets. Hamberg (1972) calculated daily prostaglandin turnover in man from the amounts of metabolites in the urine and found that therapeutic doses of aspirin, indomethacin or salicylate produced 77 to 98 percent inhibition of prostaglandin synthesis.

1.5 Adverse Effects of Salicylates

Salicylate derivatives share the therapeutic actions of reducing fever, pain and inflammation but also share several side effects. Main (1974), McGiff (1974), O'Brien (1968), Aiken (1974) and Lewis (1973) have all reported on the various side effects of aspirin including

gastro-intestional irritation, renal toxicity, inhibition of platelet aggregation and delayed and prolonged parturition.

Najjar (1977) stated that the intake of acetylsalicylic acid has been implicated in 15 percent of patients with massive gastric bleeding. Salter (1968) found that although acetylsalicylic acid inhibits the formation of hydrochloric acid per se, it increases the release of histamine, with the net result that the stimulation of gastric mucosa leads to the release of hydrochloric acid, thus increasing the potential for gastric haemmorrhage.

Hodgkin (1967) found that alcohol is also known to cause the release of histamines with the result that the concurrent use of alcohol and aspirin may percipitate gastric bleeding.

1.6 Statement of the Problem

Acetylsalicylic acid, discovered by Gilm (1859) and introduced as a therapeutic under the name of Aspirin by Dresser (1899), has enjoyed great success for a long period of time. However, medical science has looked for a superior analgesic with better tolerance, higher potency and longer duration of action.

1.7 Discovery of Diflunisal

The synthesis and evalution of five hundred salicylates at the Merck Frosst Laboratories led to the identification of a potential drug 2' , 4'-difluoro - 4 hydroxy - 3 biphenylcarboxylic acid, hereafter referred to as diflunisal.

In the first phase of the program, the acitivity-enhancing tendency of hydrophobic subsituents at the carbon-5 position was identified. The discovery of flufenisal followed in 1964. This compound was two to four times more potent than acetylsalicylic acid

and demonstrated a longer duration of action. Since gastro-intestinal tolerance was not improved, the synthetic screening effort was resumed and led to the selection of diflunisal in 1972 (Fig. 1).

The attachment of a 2', 4' - difluoro-phenyl group at the carbon-5 position of salicylic acid contributes much to the greater potency and longer duration of action by diflunisal. The ommission of the O-acetyl group, commonly present in aspirin and other active salicylates was a deliberate choice in order to avoid some of the toxic effects of this group, notably acetylation of proteins such as serum albumin and platelets.

The ability of aspirin to acetylate serum albumin and platelet membranes in vitro as well as in vivo was reported by Farr (1971) and his associates Pinckard and Hawkins (1970). The possible connection between this in vivo transacetylation and aspirin-induced toxicities - for example, asthma, anaemia, gastric haemorrhage, and platelet dysfunction - was cautioned by Farr (1970) and Krane, (1972). De Schepper (1978) demonstrated that diflunisal did not significantly increase gastro-intestinal blood loss in male subjects whereas acetylsalicylic acid did He also found no important effect on fecal blood loss when ethanol was administered with diflunisal. A significant increase in fecal blood loss was observed when acetylsalicylic acid was administered with ethanol.

Some of these potential side effects in man are not readily detectable in short term animal or clinical experiments, therefore it seemed prudent to omit the O-acetyl group from the new clinical candidate.

The selection of non-acetylated diflunisal as a candidate

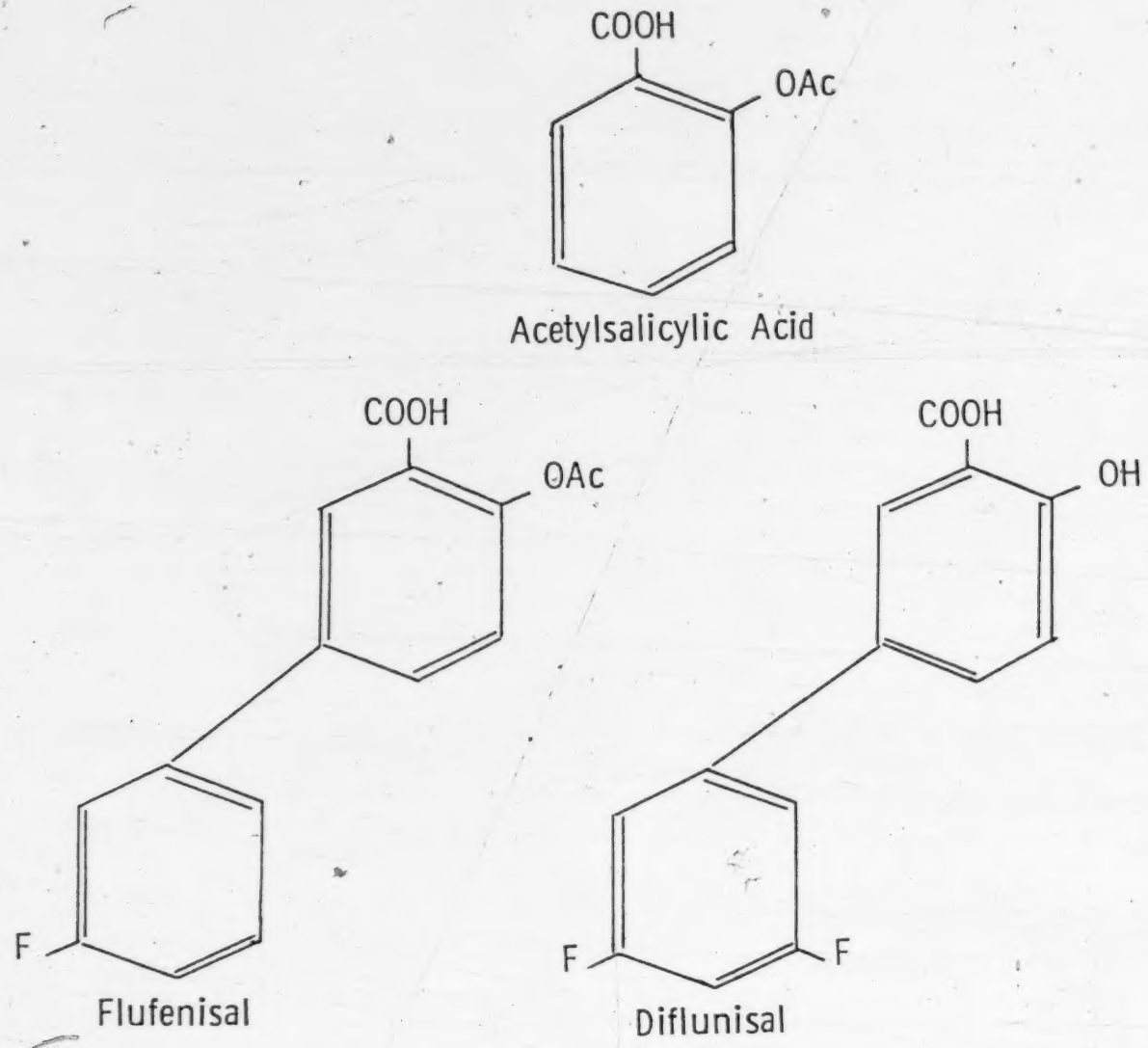

FIGURE NO. 1

Schematic Diagram of Three Salicylate Derivatives

for clinical evaluation assumed a new meaning in the light of some recent biochemical experiments. Roth et al (1975) found the inhibition of prostaglandin biosythesis by aspirin involved an irreversible acetylation of the enzyme cyclo-oxygenase. Majerus and Stanford (1971), and Patrono (1976) found that platelet enzyme appeared to be irreversibly inactivated by aspirin as was the same enzyme in sheep seminal vesicles and synovial tissues. In contrast, prostaglandin synthetase from these tissues are relatively sensitive to reversible inhibition by indomethacin and other arylacidic anti-inflammatory drugs. Unlike aspirin, diflunisal without an O-acetyl group, is incapable of acetylating cyclo-oxygenase. Majerus and Stanford (1977) found that diflunisal does not co-valently modify the enzymes as does aspirin. They hypothesized that, since diflunisal prevented aspirin from acetylating cyclo oxygenase by competitive inhibition, that both drugs acted at similar sites in preventing the biosynthesis of prostaglandins.

2.0 PURPOSE OF THIS STUDY

The object of this clinical study is to compare the safety and efficacy of difulnisal against acetylsalicylic acid in short term treatment of pain following surgical removal of impacted teeth. The results of this study may be applicable to the management of all forms of dental pain whether the pain be iatrogenic, post-treatment or of natural origin.

3.0 MATERIALS AND METHODS OF INVESTIGATION

3.1 Diflunisal: Chemical and Pharmaceutical Data

3.1.1 Physical and chemical properties:

Diflunisal is 2', 4' - difluoro - 4 hydroxy - 3 biphenylcarboxylic acid (Mol. Wt. 250.2-$C_{13}H_8O_3F_2$). It is a colourless odourless, crystalline compound which melts at 212°F. It is freely soluble in methanol and ethanol; soluble in acetone and ethyl acetate; sparingly soluble in water, chloroform, and carbon tetrachloride; and very slightly soluble in the hydrocarbon solvents.

3.1.2 Manufacturing Process:

Synthesis is carried out by reacting 2',4'-difluoronanaline with benzene to produce 2',4'-difluorobiphenyl which is then reacted with acetic anhydride to form 4-(2',4'-difluorophenyl) acetophenone. This compound is oxidized with a peracid to yield 4-(2',4'-difluorophenyl phenylacetate) which is then hydrolized to the corresponding phenol. The intermediate phenol is converted to diflunisal by reaction with carbon dioxide. The crude product thus prepared is recrystallized to yield the pure drug.

3.1.3 Dispensing Data:

Diflunisal is dispensed in peach coloured, film coated, capsule shaped tablets. In addition to diflunisal, the tablets contain fillers (pregelatinized starch and magnesium sterate) and dispersing agents (hydroxypropylcellulose and microcrystalline cellulose). The tablets are compressed and film coated, to prevent the tablet from being destroyed in the stomach.

The film coat contains hydroxypropyl methylcellulose, hydroxypropyl cellulose, talc titanium dioxide, and F.D. $\pm$ C. yellow #6 chromium lake. The tablets are polished with carnauba wax.

3.2 METHOD OF INVESTIGATION

The source of patients for this study was obtained from the office of an Oral Surgeon in Edmonton, Alberta.* A sample of sixty patients, who had undergone surgical removal of impacted teeth were randomly selected to be included in this study. The criteria for admission to the study was that the patient be between the ages of 16 and 70 and be suffering from pain developed after surgical removal of an impacted tooth or teeth.

Exclusion criteria for the study were as follows:

a. Age below 16 years or over 70 years.

b. Pregnancy or a practical probability of pregnancy.

c. Hypersensitivity to salicylates.

d. Current treatment with systemic corticosteriods or anticoagulents.

e. Active peptic ulcer or gastrointestinal haemorrhage.

f. Significant liver of kidney disease.

g. Haemopoetic disorders.

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1045 Professional Building,
Edmonton, Alberta
T5J 2B3

In order to determine if pregnancy was possible the following precautions were taken. A complete medical history was taken by the oral surgeon prior to surgery as well as a complete medical history, including haemoglobin and urinalysis taken by the patient's general physician prior to the surgical appointment.

All patients received general anaesthesia prior to undergoing surgery. The general procedure involved induction of anaesthesia by the administration of sodium pentathol, muscle relaxation with the aid of succinyl cholene and maintenance by the administration of halathane, nitrous oxide and oxygen.

This study was conducted single blind and sixty subjects were completely randomized within two treatment groups to compare the safety and efficacy of diflunisal against acetylsalicylic acid in patients with bothersome pain following oral surgery. Since the effect of acetylsalicylic acid is relatively short acting, different dose schedules had to be used for the two test agents thus making it difficult for the study to be double blind. The study was made as unbiased as possible in that the investigator recorded all parameters for safety and efficacy before asking the patient to report the times at which the medication was taken.

The patients due to undergo surgical removal of impacted teeth were given Form A (Fig. 2) to determine eligibility for the study. If the patients met all acceptable criteria and were willing to participate, sequential numbers from 31 to 90, corresponding with

FIGURE NO. 2

Forms A and C of Data Sheet

Start of treatment at onset of pain. DENTAL SURGERY FORM C

Diflunisal versus control

Investigator:

Name or initials: Study nr:

MEDICATION (please record times in 0-24 hours)

Test medication:

first dose was taken at .....hour on day of surgery

second dose was taken at .....hour on day of surgery ☐ */ day after surgery ☐

third dose was taken at ..... " ☐ " ☐

fourth dose was taken at ..... " ☐ " ☐

fifth dose was taken at ..... " ☐ " ☐

If not all doses were used, give reason:

Did patient take any other analgesic since surgery? No ; Yes

If yes, name of drug: Dose:

Time first dose was taken:

Did patient take strong alcoholic beverages No Yes If yes, specify number of glasses:

Did patient use drugs for other diseases No Yes If yes, specify:

(name + dose)

Start of treatment at onset of pain. DENTAL SURGERY FORM A

Diflunisal versus control

To be completed on day of surgery

Name or Initials:	Age: yrs.	Sex: M F	Study nr:

Procedure: Removal of impacted tooth Impacted element:

Additional surgery, if any:

Date of surgery: time Degree of trauma: mild ☐ moderate ☐ severe ☐

Anesthesia given:

Exclusion criteria for participation in the study

Please check all items:

	YES	NO
__ Age below legal consent or over 70 years.	☐	☐
__ Confirmed pregnancy or a practical possibility of pregnancy	☐	☐
__ Hypersensitivity to salicylates or to the control medication	☐	☐
__ Current treatment with: systemic corticosteroid or anticoagulants.	☐	☐
__ Active peptic ulcer or g.i. hemorrhage.	☐	☐
__ Significant liver or kidney disease.	☐	☐
__ Hemopoietic disorders.	☐	☐

If none of these conditions applies to the patient, he or she may enter the study and receive test medication + instructions for use.

numbers on the test medication, were assigned to them. The numbers were randomly assigned so that 30 subjects received diflunisal and 30 received acetylsalicylic acid.

A nurse employed by the oral surgeon and who was not involved in the evaluation of the results, gave the patient a card with instructions for use of the medication and envelopes with the medication attached to it. The card bore a number which corresponded with the test number on the eligibility form.

3.2.1. Treatment Group I (Diflunisal)

The medication for Group I (diflunisal) consisted of two envelopes containing two tablets of 250 mg diflunisal and one envelope containing one tablet of 250 mg diflunisal. Instructions to the patients were as follows:

Take the two tablets from the first envelope if bothersome pain develops.

Take the two tablets from the second envelope 6 hours later, if you still experience pain the next morning you may take the tablet from the third envelope.

The tablets should be taken with some food or a glass of water or milk.

Please do not take any other pain relieving agents between the surgery and the time that the tablets are used up.

Please avoid any excessive alcohol intake.

The use of antacids should be avoided during the time the tablets are taken. If one must be used then a product should be chosen which does not contain aluminium hydroxide.

In addition, the patients were asked to record the time (based on 0-24 hours) that the tablets in each envelope were taken. Also they were instructed to record the amount of pain present at the time of taking the first dose according to the following method of scoring:

0 = NONE.....No spontaneous pain.

1 = MILD.....Mild pain, easily tolerated.

2 = MODERATE.....Causing discomfort but bearable.

3 = SEVERE.....Causing considerable discomfort, hard to tolerate.

4 = VERY SEVERE.....Unbearable.

3.2.2 Treatment Group II (Acetylsalicylic acid)

The medication for group II (acetylsalicylic acid) consisted of one envelope containing two tablets of 500 mg acetylsalicylic acid and three envelopes containing one tablet of 500 mg acetylsalicylic acid. Instructions to the patients were as follows:

Take the two tablets from the first envelope if bothersome pain develops.

Take the tablet from the second envelope 4 hours after the first dose of medication and the tablet from the third envelope again 4 hours later, if you still experience pain the next morning you may take the tablet from the last envelope.

The tablets should be taken with some food or a glass of water or milk.

Please do not take any other pain relieving agents between the surgery and the time that the tablets are used up.

Please avoid any excessive alcohol intake.

The use of antacids should be avoided during the time the tablets are taken. If one must be used then a product should be be chosen which does not contain aluminium hydroxide.

The patients were also asked to record the time (based on 0-24 hrs) that the tablets in each envelope were taken. In addition they were to record the amount of pain present at the time of taking the first dose according to the following method of scoring:

0 = NONE .....No spontaneous pain.

1 = MILD .....Mild pain, easily tolerated.

2 = MODERATE.....Causing discomfort but bearable.

3 = SEVERE .....Causing considerable discomfort, hard to tolerate.

4 = VERY SEVERE.....Unbearable.

3.2.3 Data Recorded

Eight patients were seen the day following their surgery. There was objection by the majority of the patients to present for examination and since there was no trend developing of detectable side effects, the rest of the sample was interviewed by telephone the day following their surgery. The data was recorded by the investigator on forms A, B, and C assigned to each patient (Fig. 2 and 3).

The following data was recorded:

3.2.3.1 Pain Severity

An evaluation was made of the patients severity of spontaneous pain at the time of the investigators interview, and at the time the first dose of test medication was taken, using the rating scale given to the patient with his instructions.

DENTAL SURGERY FORM B

Start of treatment at onset of pain.

Diflunisal versus control

Name of investigator:_____

Name or initials:_____ Study nr:_____

CONTROL VISIT Evaluation on of day after surgery date:_____ hour:_____
Only to be filled in if patient took test medication.

1. PATIENTS EVALUATION

Parameters	At intake of first dose of test medication	At control visit	Description of rating scales on opposite page.
1. Pain			
11. Patient's opinion on treatment efficacy			

11. ADVERSE REACTIONS

None, or specify below:	Maximal intensity	Seriousness	Drug relationship	Action taken if any
Adverse reaction codes:	1 = mild 2 = moderate 3 = severe	1=not serious 2=serious	1=definitely not 2=probably not 3=possibly 4=probably 5=definitely	(e.g. dose reduction or discontinuation of test drug)

If adverse reaction was still present at control visit, give outcome if known (mandatory for serious reactions):

completely recovered
residual effects
reaction still present
died

patient receives treatment for reaction: yes; no
if yes, specify:_____

11. Investigator's overall evaluation taking into account expected spontaneous course of symptoms for individual patient.

Adverse reactions ↓ Efficacy →	None	Poor	Fair	Good	Excellent
No adverse reactions					
Acceptable adverse reactions					
Unacceptable adverse reactions					

Comments, if any:_____

FIGURE NO. 3

Form B of Data Sheet

3.2.3.2 Efficacy Evaluation

Subsequently, the patient and the investigator each evaluated treatment efficacy. The investigator took into account the expected spontaneous course of the signs and symptoms for the individual patient. The patients evaluation of treatment efficacy was to be rated as follows:

Score: 0 = NONE.....No good at all, ineffective drug.

1 = POOR .....Some effect, but unsatisfactory.

2 = FAIR.....Reasonable effect, but could be better.

3 = GOOD.....Satisfactory effect.

4 = EXCELLENT.....Ideal, best possible effect.

The investigator's overall evaluation of treatment efficacy (taking into account the expected spontaneous course of symptoms for the individual patient) was rated by the following method:

Score: 0 = NO EFFECT

1 = POOR EFFECT

2 = FAIR EFFECT

3 = GOOD EFFECT

4 = EXCELLENT EFFECT

3.2.3.3 Drug Acceptability

The investigator recorded his opinion as to acceptability of the drug with regard to adverse reactions using one of the following alternatives:

Score: 0 = No adverse reactions.

1 = Acceptable adverse reactions.

2 = Unacceptable adverse reactions.

Adverse reactions were reported on Form B (Fig. 3) providing data on duration, maximal intensity, seriousness, drug relationship, action taken and outcome.

Rating scales for intensity, seriousness and drug relationship were as follows:

Maximal Intensity: 1 = Mild
2 = Moderate
3 = Severe

Seriousness: 1 = Not serious
2 = Serious

A serious reaction according to the investigator's criteria was defined as any possibly related adverse experience associated with the use of subject drug which constitutes a definite hazard to the well being of the patient.

Criteria include:

1. Permanent, or for a significant period of time, inability to resume ordinary life patterns.
2. Impairment or inability to cope with future health problems.
3. Decreased life expectancy.
4. Death.

A non-serious reaction was defined as all other reactions not listed above. An opinion was recorded by the investigator as to whether reactions (if occurring) were related to the drug. Such a reaction rated in the following manner:

1 = Definitely not.

2 = Probably not.

3 = Possibly.

4 = Probably.

5 = Definitely.

3.2.4 Statistical Analysis

The data collected was statistically analyzed using the student "t" test and the chi square analysis of variance.

4.0 RESULTS AND OBSERVATIONS

The data recorded for each patient is tabulated in the appendix (Figs. 5-124). Of the original sixty patients participating in this study, eighteen were male and forty-two were female subjects (Fig.4). Six patients in Group I (diflunisal) and four patients in Group II (acetylsalicylic acid) did not complete the study according to the protocol.

In Group I (diflunisal) the six patients were excluded from the efficacy evaluation for the following reasons: patients 53 and 77 could not be contacted for the control interview; patient 47 initially took another analgesic; patients 33 and 60 found that the first dose of diflunisal did not provide significant relief of pain. These two patients changed to '292'* tablets; patient 60 in one half hour and patient 33 four hours following the first dose of diflunisal.

Diflunisal was considered a drug failure in patient 33 but not in patient 60. The latter patient did not allow sufficient time for peak plasma levels of diflunisal to be reached (T max = 2 hours) before changing medication.

Pain scores twenty four hours following surgery for these patients could not be used in the evaluation because of the use of '292'* tablets during the study period.

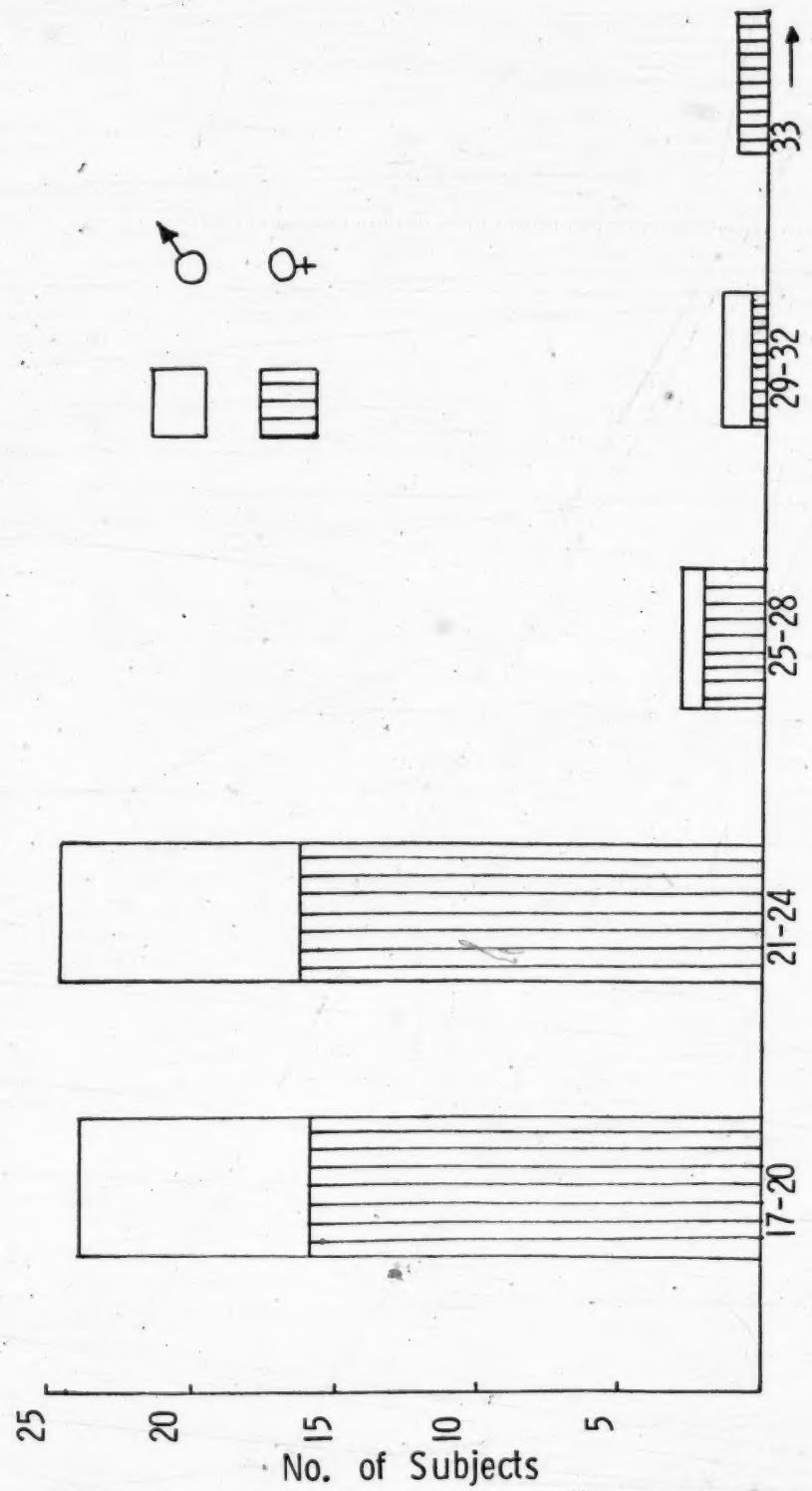
Patient 58 in Group I experienced slight nausea following the first dose of diflunisal and dropped out of the study prematurely.

The exclusion of four patients in Group II (acetylsalicylic acid) from the efficacy evaluation was for the following reasons:

* A codeine based medication manufactured by Merck-Frosst Laboratories

FIGURE NO. 4

Bar Graph Illustrating the Age and Sex Distribution of Sixty Patients



patient 90 could not be contacted for the control interview; patients 54 and 87 did not require any medication for pain; patient 78 considered the drug ineffective and 4.5 hours following the first dose discontinued medication and took a '292'* tablet.

In the case of the latter patient, acetylsalicylic acid was considered to be a drug failure since peak plasma levels of salicylates are reached within 30-60 minutes following an oral dose. A twenty four hour post surgical pain score was not considered meaningful since the patient took a '292'* tablet during the study period.

4.1 Efficacy Evaluation:

Spontaneous pain scores (post surgical pain) recorded for individuals in Tables 1 & 2 and in Summary from (Table 3) were 69 and 56 percent lower for Group I (diflunisal) and Group II (acetylsalicylic acid) respectively, at the end of the study period than immediately following surgery.

Of the patients who completed the study, patients in Group I (diflunisal) reported that they took an average of 2.6 doses, or a mean total of 1145 mg diflunisal during the study. Patients in Group II (acetylsalicylic acid) took an average of 3.6 doses or a mean total of 2290 mg acetylsalicylic acid during the study. Five patients in each treatment group found that post study medication was necessary to relieve bothersome pain and reported that they had used a '292'* tablet after the study medication had been consumed (Table 1 and 2). The evaluation of drug efficacy by patients indicates that diflunisal is more effective than acetylsalicylic acid

TABLE NO. I

DIFLUNISAL VERSUS ASA FOR PAIN FOLLOWING DENTAL SURGERY
INDIVIDUAL PATIENT DATA
GROUP I - DIFLUNISAL

Alloc. No.	Age	Sex	Degree Surgical Trauma	Post-Surgical Pain Initial	Post-Surgical Pain Control	Efficacy Patient	Efficacy Investigator	Doses Taken	Additional Medication Required Post-Study
32	17	F	Moderate	2	0	3	4	2	-
33	19	F	Moderate	3	-	0	0	1	4 hr. after 1st dose, '292'* tablets substituted
35	25	F	Moderate	2	1	4	4	3	-
38	17	M	Severe	4	1	4	4	2	-
39	19	M	Severe	2	0	3	4	3	-
41	22	F	Moderate	2	2	2	2	3	'292'
44	20	F	Moderate	2	0	4	4	2	-
46	22	F	Moderate	2	0	2	2	2	-
** 47	17	F	Moderate	-	-	-	-	-	patient started on non-study analgesic
49	19	M	Moderate	2	0	4	4	3	-
51	20	F	Severe	1	1	3	3	3	-
** 53	30	M	Moderate	-	-	-	-	-	incomplete - patient could not be contacted
55	19	F	Moderate	3	1	3	3	3	-
** 58	17	F	Moderate	2	-	-	-	1	experienced slight nausea-discontinued drug
** 60	19	M	Moderate	4	-	-	-	1	patient withdrew 0.5hr after 1st dose, "ineffective"
62	21	F	Moderate	2	4	1	1	3	'292'
64	23	F	Severe	2	1	4	4	2	-
66	19	F	Moderate	4	1	4	4	3	-
67	17	M	Moderate	2	1	3	3	3	'222'*
69	25	F	Mild	3	0	3	4	2	-
72	21	M	Moderate	4	1	3	3	3	-
74	24	F	Moderate	2	0	3	3	2	-
76	49	F	Moderate	1	2	3	3	3	-
** 77	22	M	Mild	-	-	-	-	-	incomplete - patient could not be contacted
80	20	F	Moderate	2	0	3	3	2	-
82	18	M	Moderate	4	1	4	4	2	-
83	21	F	Moderate	3	1	3	3	3	-
86	24	M	Very severe	4	0	2	2	2	'292'*
88	25	M	Severe	3	1	3	3	3	-
89	18	F	Moderate	4	2	2	3	3	-

* Trademark
** Data not included in study evaluation

TABLE NO. 2

DIFLUNISAL VERSUS ASA FOR PAIN FOLLOWING DENTAL SURGERY
INDIVIDUAL PATIENT DATA
GROUP II - ASA

Alloc. No.	Age	Sex	Degree Surgical Trauma	Post-Surgical Pain		Efficacy		Doses Taken	Additional Medication Required Post-Study
				Initial	Control	Patient	Investigator		
31	19	M	Mild	2	0	3	3	3	-
34	22	F	Moderate	3	1	3	3	4	-
36	22	F	Moderate	3	0	3	2	4	'292'*
37	21	M	Moderate	2	1	3	3	3	-
40	28	F	Moderate	3	1	3	3	3	-
42	20	F	Moderate	3	0	2	2	4	-
43	22	F	Moderate	4	2	2	1	4	-
45	22	F	Moderate	2	0	2	2	4	-
48	21	F	Moderate	4	1	4	4	4	-
50	23	M	Moderate	3	0	4	4	3	-
52	30	M	Moderate	1	1	3	3	4	-
** 54	26	F	Moderate	0	0	-	-	-	during study, patient did not require an analgesic
56	23	F	Moderate	4	2	2	1	3	'292'
57	17	F	Moderate	3	1	2	2	4	'292'
59	34	F	Moderate	1	1	3	3	4	-
61	22	M	Mild	3	2	3	3	4	-
63	23	F	Moderate	4	3	1	1	4	-
65	19	F	Moderate	2	3	2	2	4	-
68	23	F	Mild	3	3	2	2	4	-
70	18	F	Mild	4	1	1	1	4	'292'
71	19	F	Mild	2	2	1	1	4	-
73	18	F	Severe	2	3	1	0	4	-
75	23	F	Moderate	1	0	2	2	4	-
78	20	F	Moderate	3	-	0	0	1	4.5hr after 1st dose '292' tablet substituted
79	22	F	Moderate	3	2	1	1	4	-
81	31	F	Severe	1	0	3	4	2	-
84	28	M	Moderate	2	0	3	3	2	-
85	21	F	Moderate	4	1	4	4	2	-
** 87	22	M	Moderate	0	0	-	-	-	during study, patient did not require an analgesic
** 90	22	F	Mild	-	-	-	-	-	incomplete - patient could not be contacted

*Trademark
**Data not included in study evaluation

TABLE NO. 3

DIFLUNISAL VERSUS ASA FOR PAIN FOLLOWING DENTAL SURGERY

EFFICACY SUMMARY

GROUP I DIFLUNISAL

	Number	Average Age	Degree of Surgical Trauma ***	Number	Post Surgical Pain Initial	Post Surgical Pain Control	Efficacy Patient	Efficacy Investigator	Acts Slowly	Req'd Post Study Med.
Males	8	20.0	Mild	1	3	0	3	4		
Females	17	22.6	Moderate	18	2.5 ± 0.9*	1.0 ± 1.1*	2.8 ± 1.1	2.9 ± 1.1	3	3
			Severe	5	2.4 ± 1.1	0.8 ± 0.5	3.4 ± 0.6	3.6 ± 0.6		
			Very Severe	1	4	0	2	2	1	1
Total	25			25					4	4
Mean ± SD		21.8±6.2			2.6 ± 1.0*	0.8 ± 1.0*	2.9 ± 1.0	3.1 ± 1.0		

*evaluated in 17 patients, since patient 33 dropped out of study within 4 hours.
Total pain scores are a mean of 24 patients.

***number of cases

GROUP II ASA

	Number	Average Age	Degree of Surgical Trauma ***	Number	Post Surgical Pain Initial	Post Surgical Pain Control	Efficacy Patient	Efficacy Investigator	Short Duration of Action	Req'd Post Study Med.
Males	6	23.8	Mild	5	2.8 ± 0.8	1.6 ± 1.1	2.0 ± 1.0	2.0 ± 1.0		1
Females	21	22.3	Moderate	20	2.7 ± 1.0**	1.1 ± 1.0**	2.5 ± 1.0	2.3 ± 1.1	3	3
			Severe	2	1.5 ± 0.7	1.5 ± 2.1	2.0 ± 1.4	2.0 ± 2.8		
Total	27			27					3	4
Mean ± SD		22.6±4.2			2.7 ± 1.0**	1.2 ± 1.1**	2.3 ± 1.0	2.2 ± 1.1		

**evaluated in 19 patients, since patient 78 dropped out of study within 4.5 hours.
Total pain scores are a mean of 26 patients.

***number of cases

in relieving pain. Patient efficacy ratings (mean $\pm$ SD) for diflunisal and acetylsalicylic acid were 2.92 $\pm$ .997 and 2.33 $\pm$ 1.04 respectively. When the student "t" test was applied these scores were found to be statistically different at the 5 percent level of confidence and mean that the patients considered that diflunisal relieved pain satisfactorily (good) while acetylsalicylic acid was considered to have been slightly better than fair (reasonable effect, could be better). Four patients who took diflunisal felt that the drug acted slowly whereas three patients who took acetylsalicylic acid complained of its short duration of action.

As was the case with patient evaluation of drug efficacy the investigator also concludes that diflunisal is better than acetylsalicylic acid in relieving pain. The efficacy ratings (mean $\pm$ SD) for diflunisal and acetylsalicylic acid were 3.08 $\pm$ 1.04 and 2.22 $\pm$ 1.10 respectively. Using the student "t" test, these scores were found to be statistically different ($P < 0.01$) and were interpreted to mean that the performance of diflunisal was satisfactory (good) whereas that of acetylsalicylic acid was slightly better than fair and not quite satisfactory.

4.2 Adverse Experiences

Six instances of adverse reactions were reported among the Group I (diflunisal) patients, while two were reported among Group II (acetylsalicylic acid) patients. In each instance these reactions were of mild intensity and in the investigators opinion were considered as acceptable adverse experiences therefore they were classified as "not serious" (Table 4).

After the first dose of diflunisal, patients 44, 58 and 88

TABLE NO. 4

ADVERSE EXPERIENCES

DRUG TREATMENT: DIFLUNISAL

Alloc. No.	Sex	Age	Degree of Surgical Trauma	Reaction	Maximal Intensity	Seriousness	Drug Relationship	Action Taken
44	F	20	Moderate	"a little nausea after 1st dose"	mild	not serious	possibly	none
51	F	20	Severe	"nausea and drowsiness after 2nd dose"	mild	not serious	possibly	none
58	F	17	Moderate	"experienced nausea after 1st dose"	mild	not serious	possibly	patient discontinued drug
60	F	20	Moderate	"experienced nausea vomiting after 2nd dose"	mild	not serious	possibly	patient discontinued drug
83	F	21	Moderate	"nausea, vomiting, diarrhea"	mild	not serious	probably not	none
88	M	25	Severe	"slight nausea after 1st dose"	mild	not serious	probably not	none

DRUG TREATMENT: ASA

Alloc. No.	Sex	Age	Degree of Surgical Trauma	Reaction	Maximal Intensity	Seriousness	Drug Relationship	Action Taken
61	M	22	Mild	Slight headache	mild	not serious	probably not	none
84	M	28	Moderate	Slight headache, diarrhea	mild	not serious	possibly	none

experienced slight nausea. Patient 51 experienced nausea and drowsiness after the second dose. Patient 58 discontinued the drug after the first dose, patient 80 discontinued the drug after the second dose. The investigator considered four of the adverse reactions to be possibly related to diflunisal, two reactions were considered to be probably not related to the drug.

After the first dose of acetylsalicylic acid, two patients (61 and 84) reported the development of a "slight headache". One reaction was considered to be possibly drug related, the other was considered to be probably not related.

These reactions do not appear to be related to the degree of surgical trauma, and the symptoms reported are more consistent with side effects following general anaesthesia.

5.0 DISCUSSION

The surgical removal of impacted dental units is a suitable test method for evaluating the efficacy and tolerance of an analgesic. A sample can be selected to be reasonably homogenous as to age, type of surgery and amount of trauma to hard and soft tissues. The statistical analysis, therefore, may discover differences in response of the sample that are related to the test agent.

There are, however, individual factors which cannot be measured or controlled in any study of this type. These include variations in pain perception, pain threshold and the emotional status of varied environmental stress to which the patient may be subjected.

Variations such as these were noted in this study when the patient responses were recorded. Some of the subjects were very clear and co-operative in giving their responses during the interview. Others were less clear and unconcerned about providing accurate recordings. In these instances it was difficult for the investigator to be objective.

Diflunisal is found to be more effective than acetylsalicylic acid in reducing pain following surgical removal of impacted teeth. The mean efficacy rating by the patient for Group I (diflunisal) was 2.19 ± 1.00 as compared with the rating of 2.33 ± 1.04 for Group II (acetylsalicylic acid). This difference is significant at the 5 percent level of confidence (Table 5) as revealed by Student "t" test.

The mean efficacy rating by the investigator for Group I (diflunisal) was 3.08 ± 1.04 compared with the ratings of 2.22 ± 1.10

TABLE NO. 5

Efficacy Ratings of Diflunisal

Versus A.S.A.

Efficacy	Patient Rating				Investigator Rating			
	Diflunisal		A.S.A.		Diflunisal		A.S.A.	
0 None	1	(4%)	1	(3.6%)	1	(4%)	2	(3.6%)
1 Poor	1	(4%)	5	(19.2%)	1	(4%)	6	(22.2%)
2 Fair	4	(16%)	8	(29.8%)	3	(12%)	7	(30.5%)
3 Good	12	(48%)	10	(36.3%)	10	(40%)	8	(29.8%)
4 Excellent	7	(28%)	3	(11.1%)	10	(40%)	4	(14.9%)
Total No.	25	(100%)	27	(100%)	25	(100%)	27	(100%)

for Group II (acetylsalicylic acid). Analysis by the use of the student "t" test shows this difference to be significant at the 1 percent level of confidence.

The above results are in accordance with previous findings by Wes (1978) who compared the efficacy of diflunisal versus placebo and glafenine in the treatment of pain following surgical removal of mandibular third molars. Barrau (1978) in his study comparing the efficacy of diflunisal versus oxyphenbutaxone in the treatment of sprains of the ankle found diflunisal to be an effective analgesic agent. Van Winzom and Rodda (1977) compared the efficacy of diflunisal versus glafenine and acetylsalicylic acid in patients suffering pain following oral or orthopedic surgery. They found diflunisal to be effective in relieving post operative pain in 75-85 percent of patients.

The relationship of the degree of trauma and the amount of initial pain following surgery (Tables 6 and 7) to drug efficacy is not statistically significant according to the chi square analysis of variance ($p > 0.5$). Sveen and Gilhous-Moe (1975) reported in their study that there was no relationship between degree of trauma and pain intensity.

A sex difference in response to drug efficacy has been discovered in this study. When sex, but not drug, is correlated with the efficacy rating of both drugs it is noted that the male subjects achieve more relief from drug therapy than do the female subjects. The males reported a mean efficacy rating of 3.62 as compared to a rating of 2.41 for the females (Table 8). The same feature is found

TABLE NO. 6

Pain Levels as Described by the Patient

Level of Pain	Initial Evaluation				Interview Evaluation			
	Diflunisal		A.S.A.		Diflunisal		A.S.A.	
0 None	0	(0%)	0	(0%)	4	(33.3%)	8	(29.6%)
1 Mild	2	(7.4%)	4	(14.8%)	11	(40.7%)	9	(33.3%)
2 Moderate	13	(48.1%)	7	(26%)	3	(11.1%)	5	(18.5%)
3 Severe	5	(18.5%)	10	(37%)	0	(0%)	4	(14.8%)
4 Very Severe	7	(26%)	6	(22.2%)	1	(3.7%)	0	(0%)
Total No.	27	(100%)	27	(100%)	24*	(88.8%)	26**	(96.2%)

* Three patients discontinued the study after taking one dose of diflunisal.

** One patient discontinued the study after taking one dose of A.S.A.

TABLE NO. 7

Degree of Surgical Trauma

as Rated by the Oral Surgeon

Degree of Surgical Trauma	No. of Patients			
	Group I (Diflunisal)		Group II (A.S.A.)	
1 Mild	2	(6.7%)	6	(20%)
2 Moderate	22	(73.3%)	22	(73.3%)
3 Severe	5	(16.7%)	2	(6.7%)
4 Very Severe	1	(3.3%)	0	(0%)
Total No.	30	(100%)	30	(100%)

TABLE NO. 8

Efficacy Ratings by the Patient of Diflunisal

Versus A.S.A. Grouped According to Sex

Efficacy Rating	Males				Females			
	Diflunisal		A.S.A.		Diflunisal		A.S.A.	
0 None	0	(0%)	0	(0%)	1	(5.8%)	1	(4.7%)
1 Poor	0	(0%)	0	(0%)	1	(5.8%)	5	(23.9%)
2 Fair	1	(12.5%)	0	(0%)	3	(17.7%)	8	(38.1%)
3 Good	4	(50%)	5	(83.3%)	8	(47.1%)	5	(23.9%)
4 Excellent	3	(37.5%)	1	(16.7%)	4	(23.6%)	2	(9.4%)
Total No.	8	(100%)	6	(100%)	17	(100%)	21	(100%)

to be present on the efficacy ratings recorded by the investigator. The mean efficacy rating for the males was 3.30 and for the females was 2.41 (Table 9).

Sex differences in response to pain have been reported in the literature previously by Hardy (1952), Kennard (1952) and Merskey and Spear (1964). Kennard was able to show that the lower pain threshold in females was not due to any significant difference in skin thickness. Hardy stated that pain threshold is highly correlated with pain reaction threshold and that both measures are lower in females.

Diflunisal is not found to be more effective than acetylsalicylic acid in the male subjects. Even though the males in total received more satisfaction from both drugs, the student "t" test showed the difference between the two groups to be not significant ($p > 0.8$). The mean patient efficacy rating was $3.23 \pm .71$ for Group I (diflunisal) and $3.20 \pm .45$ for Group II (acetylsalicylic acid). The same finding applies to the efficacy ratings recorded by the investigator. These were $3.37 \pm .74$ for Group I (diflunisal) and $3.20 \pm .45$ for Group II (acetylsalicylic acid).

Diflunisal was found to be more effective than acetylsalicylic acid in the female subjects. Although females experienced less relief overall than did the males there was a significant difference between the efficacy ratings for Group I (diflunisal) and Group II (acetylsalicylic acid). The mean female patient efficacy rating was 2.76 ± 1.09 for Group I and 2.14 ± 1.06 for Group II. The student

TABLE NO. 9

Efficacy Ratings by the Investigator

of Diflunisal Versus A.S.A. Grouped

According to Sex

Efficacy Rating	Males		Females	
	Diflunisal	A.S.A.	Diflunisal	A.S.A.
0 None	0 (0%)	0 (0%)	1 (5.8%)	2 (9.4%)
1 Poor	0 (0%)	0 (0%)	1 (5.8%)	6 (28.6%)
2 Fair	1 (12.5%)	0 (0%)	2 (11.6%)	7 (33.3%)
3 Good	3 (37.5%)	5 (83.3%)	7 (41.4%)	3 (14.3%)
4 Excellent	4 (50%)	1 (16.7%)	6 (35.6%)	3 (14.3%)
Total No.	8 (100%)	6 (100%)	17 (100%)	21 (100%)

"t" test indicates a significant difference at the 7 percent level of confidence. The mean investigator efficacy rating was 2.94 $\pm$ 1.20 for Group I and 2.00 $\pm$ 1.20 for Group II. This difference is significant at the 2 percent level of confidence.

Although sex differences in response to pain have been documented, the results of this study may be due in part to the small number of males (14) as compared to the number of females (38). The imbalance in numbers may have had some bearing on the results.

Six subjects in Group I (diflunisal) experienced one or more adverse reactions as compared with two subjects in Group II (acetylsalicylic acid). The chi square analysis of variance showed that the difference between the groups was not significant ($p > 0.1$) although a trend was indicated (Table 10). There were nine experiences of nausea, vomitting and diarrhoea in Group I (diflunisal) as compared to only one experience of diarrhoea in Group II (acetylsalicylic acid). This result does not substantiate the claims of the manufacturer that diflunisal is more easily tolerated than acetylsalicylic acid nor that of Stone (1977) who found that single or subacute doses of diflunisal produced less apparent irritation of the gastric mucosa than did similar doses of aspirin.

Although only a trend indicates that diflunisal was less tolerated in this study than was acetylsalicylic acid further investigation should be undertaken. The small number of subjects in this study may not provide a true indication of the safety factor of diflunisal. A study utilizing a larger sample size may provide further insight into this problem.

TABLE NO. 10

Total Adverse Reactions Experienced

by the Patients

Adverse Reactions	Treatment	
	Diflunisal (25 patients)	A. S. A. (27 patients)
None	19	25
Nausea	6	0
Vomitting	2	0
Diarrhea	1	1
Headache	0	2
Drowsiness	1	0
Total No.	29*	28*

* Some patients experienced more than one adverse reaction.

When the sample was grouped according to sex it was found that six females in Group I (diflunisal) experienced adverse reactions as compared with one female in Group II (acetylsalicylic acid) Table 4. The chi square analysis of variance showed this difference to be significant at the 5 percent level of confidence. There was no such difference recorded in the male subjects.

6.0 SUMMARY AND CONCLUSIONS

A single blind and completely randomized study was undertaken in order to compare the efficacy and safety of diflunisal against acetylsalicylic acid. Sixty patients who had undergone surgical removal of impacted teeth were included in the study.

Evaluation of efficacy and adverse reactions were recorded by the patient and by the investigator and the results subjected to a statistical analysis using the student "t" test and the chi square analysis of variance. The following conclusions were drawn:

6.1 Diflunisal was found to be more effective than acetylsalicylic acid in reducing pain following surgical removal of impacted teeth.

6.2 Males received greater relief from both analgesics but did not receive greater relief from diflunisal than from acetylsalicylic acid.

6.3 Females received less relief from both analgesics than did males but reported diflunisal superior to acetylsalicylic acid.

6.4 The age of the patient, degree of sugical trauma to hard and soft tissues and the amount of initial pain following surgery was not found to be significant in evaluating drug efficacy.

6.5 No significant difference in adverse reaction experience was observed between diflunisal and acetysalicylic acid, when only drug, but not sex, was considered.

6.6 Diflunisal caused a significantly greater incidence of adverse reaction experience in the female subjects than did acetylsalicylic acid.

6.7 All of the adverse reactions reported were of mild intensity, short duration and recorded as not serious by the investigator.

The results indicating a sex difference with regard to efficacy and safety of the test analgesics were of particular interest. It is recommended that further studies be undertaken utilizing a larger sample size of each sex to more fully elucidate this finding.

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8.0 APPENDIX

Start of treatment at onset of pain. DENTAL SURGERY FORM A

Diflunisal versus control

To be completed on day of surgery

Name or Initials: J.M.	Age: 19 yrs.	Sex: M F	Study nr: 31

Procedure: Removal of impacted tooth Impacted element: 38, 48.

Additional surgery, if any: 18, 28.

Date of surgery: sept. 9 time ~~8~~ Degree of trauma: mild ☒ moderate ☐ severe ☐

Anesthesia given: general

Exclusion criteria for participation in the study

Please check all items:

	YES	NO
__ Age below legal consent or over 70 years.	☐	☒
__ Confirmed pregnancy or a practical possibility of pregnancy	☐	☒
__ Hypersensitivity to salicylates or to the control medication	☐	☒
__ Current treatment with: systemic corticosteroid or anticoagulants.	☐	☒
__ Active peptic ulcer or g.i. hemorrhage.	☐	☒
__ Significant liver or kidney disease.	☐	☒
__ Hemopoietic disorders.	☐	☒

If none of these conditions applies to the patient, he or she may enter the study and receive test medication + instructions for use.

Start of treatment at onset of pain. DENTAL SURGERY FORM C

Diflunisal versus control

Investigator: Dr. M.L. McCUE

Name or initials: J.M. Study nr: 31

MEDICATION (please record times in 0-24 hours)

Test medication:

first dose was taken at 1800 hour on day of surgery

second dose was taken at 2200 hour on day of surgery ☒ / day after surgery ☐

third dose was taken at	0130	-	☐	-	☒
fourth dose was taken at	.....	-	☐	-	☐
fifth dose was taken at	.....	-	☐	-	☐

If not all doses were used, give reason: no further medication required

Did patient take any other analgesic since surgery? No ; Yes

If yes, name of drug: Dose:

Time first dose was taken:

Did patient take strong alcoholic beverages No X Yes If yes, specify number of glasses:

Did patient use drugs for other diseases No X Yes If yes, specify: (name + dose)

FIGURE 5

DENTAL SURGERY FORM B

Start of treatment at onset of pain.

Diflunisal versus control

Name of investigator: Dr. M.L. McCUE

Name or initials: J.M. Study nr: 37

CONTROL VISIT Evaluation on of day after surgery date: sept. 10 hour: 1500
Only to be filled in if patient took test medication.

1. PATIENTS EVALUATION

Parameters	At intake of first dose of test medication	At control visit	Description of rating scales on opposite page.
1. Pain	2	0	
11. Patient's opinion on treatment efficacy		3	

11. ADVERSE REACTIONS

No or specify below:	Maximal intensity	Seriousness	Drug relationship	Action taken if any
Adverse reaction codes:	1 = mild 2 = moderate 3 = severe	1=not serious 2=serious	1=definitely not 2=probably not 3=possibly 4=probably 5=definitely	(e.g. dose reduction or discontinuation of test drug)

If adverse reaction was still present at control visit, give outcome if known (mandatory for serious reactions):

completely recovered
residual effects
reaction still present
died

patient receives treatment for reaction: yes; no
if yes, specify: _____

11. Investigator's overall evaluation taking into account expected spontaneous course of symptoms for individual patient.

Adverse reactions	Efficacy → None	Poor	Fair	Good	Excellent
No adverse reactions	0			X	
Acceptable adverse reactions					
Unacceptable adverse reactions					

Comments, if any: _____

FIGURE 6

Start of treatment at onset of pain. DENTAL SURGERY FORM A

Diflunisal versus control

To be completed on day of surgery

Name or Initials: C.W.	Age: 17 yrs.	Sex: F M	Study nr: 32

Procedure: Removal of impacted tooth Impacted element: 38, 48.

Additional surgery, if any: none

Date of surgery: sept. 9 Time: a.m. Degree of trauma: mild ☐ moderate ☒ severe ☐

Anesthesia given: general

Exclusion criteria for participation in the study

Please check all items:

	YES	NO
__ Age below legal consent or over 70 years.	☐	☒
__ Confirmed pregnancy or a practical possibility of pregnancy	☐	☒
__ Hypersensitivity to salicylates or to the control medication	☐	☒
__ Current treatment with: systemic corticosteroid or anticoagulants.	☐	☒
__ Active peptic ulcer or g.i. hemorrhage.	☐	☒
__ Significant liver or kidney disease.	☐	☒
__ Hemopoietic disorders.	☐	☒

If none of these conditions applies to the patient, he or she may enter the study and receive test medication + instructions for use.

Start of treatment at onset of pain. DENTAL SURGERY FORM C

Diflunisal versus control Dr. M.L. McGUE

Investigator:

Name or initials: C.W. Study nr: 32

MEDICATION (please record times in 0-24 hours)

Test medication:

first dose was taken at 1630 .....hour on day of surgery

second dose was taken at 0100 hour on day of surgery ☐ °/ day after surgery ☒

third dose was taken at ..... - ☐ - ☐

fourth dose was taken at ..... - ☐ - ☐

fifth dose was taken at ..... - ☐ - ☐

If not all doses were used, give reason: no further doses required for pain

Did patient take any other analgesic since surgery? No ☒ ; Yes ☐

If yes, name of drug: Dose:

Time first dose was taken:

Did patient take strong alcoholic beverages No X Yes ☐ If yes, specify number of glasses:

Did patient use drugs for other diseases No X Yes ☐ If yes, specify: (name + dose)

FIGURE 7

DENTAL SURGERY FORM B

Start of treatment at onset of pain.

Diflunisal versus control

Name of investigator: Dr. M.L. McCUE

Name or initials: C.W. Study nr: 32

CONTROL VISIT Evaluation on of day after surgery date: sept. 10 hour: 1300
Only to be filled in if patient took test medication.

1. PATIENTS EVALUATION

Parameters	At intake of first dose of test medication	At control visit	Description of rating scales on opposite page.
1. Pain	2	0	
11. Patient's opinion on treatment efficacy		3	

11. ADVERSE REACTIONS

None or specify below:	Maximal intensity	Seriousness	Drug relationship	Action taken if any
Adverse reaction codes:	1 = mild 2 = moderate 3 = severe	1=not serious 2=serious	1=definitely not 2=probably not 3=possibly 4=probably 5=definitely	(e.g. dose reduction or discontinuation of test drug)

If adverse reaction was still present at control visit, give outcome if known (mandatory for serious reactions):

completely recovered
residual effects
reaction still present
died

patient receives treatment for reaction: yes; no
if yes, specify: _____

11. Investigator's overall evaluation taking into account expected spontaneous course of symptoms for individual patient.

Adverse reactions	Efficacy →	None	Poor	Fair	Good	Excellent
No adverse reactions	0					x
Acceptable adverse reactions						
Unacceptable adverse reactions						

Comments, if any: _____

FIGURE 8

Start of treatment at onset of pain. DENTAL SURGERY FORM A

Diflunisal versus control

To be completed on day of surgery

Name or Initials: S.M.	Age: 19 yrs.	Sex: F M	Study nr: 33

Procedure: Removal of impacted tooth Impacted element: 18, 28, 38, 48.

Additional surgery, if any: none

Date of surgery: sept.9 time p.m. Degree of trauma: mild ☐ moderate X ☐ severe ☐

Anesthesia given: general

Exclusion criteria for participation in the study

Please check all items:

	YES	NO
__ Age below legal consent or over 70 years.	☐	X
__ Confirmed pregnancy or a practical possibility of pregnancy	☐	X
__ Hypersensitivity to salicylates or to the control medication	☐	X
__ Current treatment with: systemic corticosteroid or anticoagulants.	☐	X
__ Active peptic ulcer or g.i. hemorrhage.	☐	X
__ Significant liver or kidney disease.	☐	X
__ Hemopoietic disorders.	☐	X

If none of these conditions applies to the patient, he or she may enter the study and receive test medication + instructions for use.

Start of treatment at onset of pain. DENTAL SURGERY FORM C

Diflunisal versus control

Investigator: Dr. M.L. McCUE

Name or initials: S.M. Study nr: 33

MEDICATION (please record times in 0-24 hours)

Test medication:

first dose was taken at 1600 hour on day of surgery

second dose was taken at .....hour on day of surgery ☐ */ day after surgery ☐

third dose was taken at ..... - ☐ - ☐

fourth dose was taken at ..... - ☐ - ☐

fifth dose was taken at ..... - ☐ - ☐

If not all doses were used, give reason: the first was not effective so the patient did not take any further doses of test medication

Did patient take any other analgesic since surgery? No ; YeXX

If yes, name of drug: 292 Dose: 1 tab

Time first dose was taken: 2030 hrs sept.9

Did patient take strong alcoholic beverages No X Yes If yes, specify number of glasses:

Did patient use drugs for other diseases No X Yes If yes, specify: (name + dose)

FIGURE 9

DENTAL SURGERY FORM B

Start of treatment at onset of pain.

Diflunisal versus control

Name of investigator: Dr. M.L. McCUE

Name or initials: S.M. Study nr: 33

CONTROL VISIT Evaluation on of day after surgery date: sept.10 hour: 2100
Only to be filled in if patient took test medication.

1. PATIENTS EVALUATION

Parameters	At intake of first dose of test medication	At control visit	Description of rating scales on opposite page.
1. Pain	3	0	
11. Patient's opinion on treatment efficacy		0	

11. ADVERSE REACTIONS

No~~AR~~ or specify below:	Maximal intensity	Seriousness	Drug relationship	Action taken if any
Adverse reaction codes:	1 = mild 2 = moderate 3 = severe	1=not serious 2=serious	1=definitely not 2=probably not 3=possibly 4=probably 5=definitely	(e.g. dose reduction or discontinuation of test drug)

If adverse reaction was still present at control visit, give outcome if known (mandatory for serious reactions):

completely recovered
residual effects
reaction still present
died

patient receives treatment for reaction: yes; no
if yes, specify:

11. Investigator's overall evaluation taking into account expected spontaneous course of symptoms for individual patient.

Adverse reactions	Efficacy → None	Poor	Fair	Good	Excellent
No adverse reactions	0 x				
Acceptable adverse reactions					
Unacceptable adverse reactions					

Comments, if any: the patient discontinued the drug after taking one dose. She felt that the drug was not effective at all

FIGURE 10

Start of treatment at onset of pain. DENTAL SURGERY FORM A

Diflunisal versus control

To be completed on day of surgery

Name or Initials: D.T.	Age: 22 yrs.	Sex: F (M / F)	Study nr: 34

Procedure: Removal of impacted tooth Impacted element: 18, 28, 38, 48.

Additional surgery, if any: none

Date of surgery: sept. 14 time 8 A.M. Degree of trauma: mild ☐ moderate ☒ severe ☐

Anesthesia given: general

Exclusion criteria for participation in the study

Please check all items:

	YES	NO
__ Age below legal consent or over 70 years.	☐	☒
__ Confirmed pregnancy or a practical possibility of pregnancy	☐	☒
__ Hypersensitivity to salicylates or to the control medication	☐	☒
__ Current treatment with: systemic corticosteroid or anticoagulants.	☐	☒
__ Active peptic ulcer or g.i. hemorrhage.	☐	☒
__ Significant liver or kidney disease.	☐	☒
__ Hemopoietic disorders.	☐	☒

If none of these conditions applies to the patient, he or she may enter the study and receive test medication + instructions for use.

Start of treatment at onset of pain. DENTAL SURGERY FORM C

Diflunisal versus control Dr. M.L. McCUE

Investigator:

Name or initials: D.T. Study nr: 34

MEDICATION (please record times in 0-24 hours)

Test medication:

first dose was taken at	1115	hour on day of surgery			
second dose was taken at	1500	hour on day of surgery ☐	*/ day after surgery ☐		
third dose was taken at	1900	-	☒	-	☐
fourth dose was taken at	0130	-	☐	-	☒
fifth dose was taken at	.....	-	☐	-	☐

If not all doses were used, give reason:

Did patient take any other analgesic since surgery? ☒ No ; Yes

If yes, name of drug: Dose:

Time first dose was taken:

Did patient take strong alcoholic beverages ☒ No Yes If yes, specify number of glasses:

Did patient use drugs for other diseases ☒ No Yes If yes, specify: (name + dose)

FIGURE 11

DENTAL SURGERY FORM B

Start of treatment at onset of pain.

Diflunisal versus control

Name of investigator: Dr. M.L. McCUE

Name or initials: D.T. Study nr: 34

CONTROL VISIT Evaluation on of day after surgery date: sept. 15 hour: 1215
Only to be filled in if patient took test medication.

1. PATIENTS EVALUATION

Parameters	At intake of first dose of test medication	At control visit	Description of rating scales on opposite page.
1. Pain	3	1	
11. Patient's opinion on treatment efficacy		3	

11. ADVERSE REACTIONS

None ~~xxxx~~ specify below:	Maximal intensity	Seriousness	Drug relationship	Action taken if any
Adverse reaction codes:	1 = mild 2 = moderate 3 = severe	1=not serious 2=serious	1=definitely not 2=probably not 3=possibly 4=probably 5=definitely	(e.g. dose reduction or discontinuation of test drug)

If adverse reaction was still present at control visit, give outcome if known (mandatory for serious reactions):

completely recovered
residual effects
reaction still present
died

patient receives treatment for reaction: yes; no
if yes, specify:

11. Investigator's overall evaluation taking into account expected spontaneous course of symptoms for individual patient.

Adverse reactions	Efficacy →	None	Poor	Fair	Good	Excellent
No adverse reactions	0				X	
Acceptable adverse reactions						
Unacceptable adverse reactions						

Comments, if any:

FIGURE 12

Start of treatment at onset of pain. DENTAL SURGERY FORM A

Diflunisal versus control

To be completed on day of surgery

Name or Initials: S.G.	Age: 25 yrs.	Sex: M / F	Study nr: 35

Procedure: Removal of impacted tooth Impacted element: 18, 28, 38, 48.

Additional surgery, if any: none

Date of surgery: sept. 14 time a.m. Degree of trauma: mild ☐ moderate ☒ severe ☐

Anesthesia given: general

Exclusion criteria for participation in the study

Please check all items:

	YES	NO
__ Age below legal consent or over 70 years.	☐	☒
__ Confirmed pregnancy or a practical possibility of pregnancy	☐	☒
__ Hypersensitivity to salicylates or to the control medication	☐	☒
__ Current treatment with: systemic corticosteroid or anticoagulants.	☐	☒
__ Active peptic ulcer or g.i. hemorrhage.	☐	☒
__ Significant liver or kidney disease.	☐	☒
__ Hemopoietic disorders.	☐	☒

If none of these conditions applies to the patient, he or she may enter the study and receive test medication + instructions for use.

Start of treatment at onset of pain. DENTAL SURGERY FORM C

Diflunisal versus control

Investigator: Dr. M.L. McCUE

Name or initials: S.G. Study nr: 35

MEDICATION (please record times in 0-24 hours)

Test medication:

first dose was taken at 1245 ...hour on day of surgery

second dose was taken at 1845 ...hour on day of surgery ☒ */ day after surgery ☐

third dose was taken at 0815 - ☐ - ☒

fourth dose was taken at ..... - ☐ - ☐

fifth dose was taken at ..... - ☐ - ☐

If not all doses were used, give reason:

Did patient take any other analgesic since surgery? ☒ No ; Yes

If yes, name of drug: Dose:

Time first dose was taken:

Did patient take strong alcoholic beverages? ☒ No Yes If yes, specify number of glasses:

Did patient use drugs for other diseases ☒ No Yes If yes, specify: (name + dose)

FIGURE 13

DENTAL SURGERY FORM B

Start of treatment at onset of pain.

Diflunisal versus control

Name of investigator: Dr. M.L. McCUE

Name or initials: S.G. Study nr: 35

CONTROL VISIT Evaluation on of day after surgery date: sept. 15 hour: 1900
Only to be filled in if patient took test medication.

1. PATIENTS EVALUATION

Parameters	At intake of first dose of test medication	At control visit	Description of rating scales on opposite page.
1. Pain	2	1	
11. Patient's opinion on treatment efficacy		4	

11. ADVERSE REACTIONS

None or specify below:	Maximal intensity	Seriousness	Drug relationship	Action taken if any
Adverse reaction codes:	1 = mild 2 = moderate 3 = severe	1=not serious 2=serious	1=definitely not 2=probably not 3=possibly 4=probably 5=definitely	(e.g. dose reduction or discontinuation of test drug)

If adverse reaction was still present at control visit, give outcome if known (mandatory for serious reactions):

completely recovered
residual effects
reaction still present
died

patient receives treatment for reaction: yes; no
if yes, specify:

11. Investigator's overall evaluation taking into account expected spontaneous course of symptoms for individual patient.

Adverse reactions	Efficacy →	None	Poor	Fair	Good	Excellent
No adverse reactions	0					X
Acceptable adverse reactions						
Unacceptable adverse reactions						

Comments, if any: patient was very happy with the medication
a slight sensation of drowsiness occurred

FIGURE 14

Start of treatment at onset of pain. DENTAL SURGERY FORM A

Diflunisal versus control

To be completed on day of surgery

Name or Initials: L.W.	Age: 22 yrs.	Sex: M F	Study nr: 36

Procedure: Removal of impacted tooth Impacted element: 18, 28, 38, 48.

Additional surgery, if any: none

Date of surgery: sept.14 time a.m. Degree of trauma: mild ☐ moderate ☒ severe ☐

Anesthesia given: general

Exclusion criteria for participation in the study

Please check all items:

	YES	NO
__ Age below legal consent or over 70 years.	☐	☒
__ Confirmed pregnancy or a practical possibility of pregnancy	☐	☒
__ Hypersensitivity to salicylates or to the control medication	☐	☒
__ Current treatment with: systemic corticosteroid or anticoagulants.	☐	☒
__ Active peptic ulcer or g.i. hemorrhage.	☐	☒
__ Significant liver or kidney disease.	☐	☒
__ Hemopoietic disorders.	☐	☒

If none of these conditions applies to the patient, he or she may enter the study and receive test medication + instructions for use.

Start of treatment at onset of pain. DENTAL SURGERY FORM C

Diflunisal versus control

Investigator: Dr. M.L. McCUE

Name or initials: L.W. Study nr: 36

MEDICATION (please record times in 0-24 hours)

Test medication:

first dose was taken at 1200 hour on day of surgery

second dose was taken at 1600 hour on day of surgery ☒ / day after surgery ☐

third dose was taken at	2100	-	☒	-	☐
fourth dose was taken at	0300	-	☐	-	☒
fifth dose was taken at	.....	-	☐	-	☐

If not all doses were used, give reason:

Did patient take any other analgesic since surgery? No : ~~Yes~~ after study

If yes, name of drug: 292 Dose: 1 tab

Time first dose was taken: sept.15 1400hrs

Did patient take strong alcoholic beverages? ☒ No Yes If yes, specify number of glasses:

Did patient use drugs for other diseases ☒ No Yes If yes, specify:

(name + dose)

FIGURE 15

DENTAL SURGERY FORM B

Start of treatment at onset of pain.
Diflunisal versus control
Name of investigator: Dr. M.L. McCUE

Name or initials: L.W. Study nr: 36

CONTROL VISIT Evaluation on of day after surgery date: sept.15 hour: 1800
Only to be filled in if patient took test medication.

1. PATIENTS EVALUATION

Parameters	At intake of first dose of test medication	At control visit	Description of rating scales on opposite page.
1. Pain	3	0	
11. Patient's opinion on treatment efficacy		3	

11. ADVERSE REACTIONS

None or specify below:	Maximal intensity	Seriousness	Drug relationship	Action taken if any
Adverse reaction codes:	1 = mild 2 = moderate 3 = severe	1=not serious 2=serious	1=definitely not 2=probably not 3=possibly 4=probably 5=definitely	(e.g. dose reduction or discontinuation of test drug)

If adverse reaction was still present at control visit, give outcome if known (mandatory for serious reactions):

completely recovered
residual effects
reaction still present
died

patient receives treatment for reaction: yes; no
if yes, specify:

11. Investigator's overall evaluation taking into account expected spontaneous course of symptoms for individual patient.

Adverse reactions	Efficacy →	None	Poor	Fair	Good	Excellent
No adverse reactions	0			X		
Acceptable adverse reactions						
Unacceptable adverse reactions						

Comments, if any: duration of relief not too long , patient took a 292 after the study was completed

FIGURE 16

Start of treatment at onset of pain. DENTAL SURGERY FORM A

Diflunisal versus control

To be completed on day of surgery

Name or Initials: B.L.	Age: 21 yrs.	Sex: M ☒ F ☐	Study nr: 37

Procedure: Removal of impacted tooth Impacted element: 18, 38, 48.

Additional surgery, if any: none

Date of surgery: sept. 14 time ____ Degree of trauma: mild ☐ moderate ☒x severe ☐

Anesthesia given: general

Exclusion criteria for participation in the study

Please check all items:

	YES	NO
___ Age below legal consent or over 70 years.	☐	☒
___ Confirmed pregnancy or a practical possibility of pregnancy	☐	☒
___ Hypersensitivity to salicylates or to the control medication	☐	☒
___ Current treatment with: systemic corticosteroid or anticoagulants.	☐	☒
___ Active peptic ulcer or g.i. hemorrhage.	☐	☒
___ Significant liver or kidney disease.	☐	☒
___ Hemopoietic disorders.	☐	☒

If none of these conditions applies to the patient, he or she may enter the study and receive test medication + instructions for use.

Start of treatment at onset of pain. DENTAL SURGERY FORM C

Diflunisal versus control

Investigator: Dr. M.L. McCUE

Name or Initials: B.L. Study nr: 37

MEDICATION (please record times in 0-24 hours)

Test medication:

first dose was taken at 1430 hour on day of surgery

second dose was taken at 1850 hour on day of surgery ☒ */ day after surgery ☐

third dose was taken at 2310 - ☒ - ☐

fourth dose was taken at ..... - ☐ - ☐

fifth dose was taken at ..... - ☐ - ☐

If not all doses were used, give reason: did not require the final dose

Did patient take any other analgesic since surgery? ☒No ; Yes

If yes, name of drug: ____ Dose: ____

Time first dose was taken: ____

Did patient take strong alcoholic beverages? ☒No Yes If yes, specify number of glasses: ____

Did patient use drugs for other diseases ☒No Yes If yes, specify: ____ (name + dose) ____

FIGURE 17

DENTAL SURGERY FORM B

Start of treatment at onset of pain.

Diflunisal versus control

Name of investigator: Dr. M.L. McCUE

Name or initials: B.L. Study nr: 37

CONTROL VISIT Evaluation on of day after surgery date: sept.15 hour: 1230
Only to be filled in if patient took test medication.

1. PATIENTS EVALUATION

Parameters	At intake of first dose of test medication	At control visit	Description of rating scales on opposite page.
1. Pain	2	1	
11. Patient's opinion on treatment efficacy		3	

11. ADVERSE REACTIONS

None xxx or specify below:	Maximal intensity	Seriousness	Drug relationship	Action taken if any
Adverse reaction codes:	1 = mild 2 = moderate 3 = severe	1=not serious 2=serious	1=definitely not 2=probably not 3=possibly 4=probably 5=definitely	(e.g. dose reduction or discontinuation of test drug)

If adverse reaction was still present at control visit, give outcome if known (mandatory for serious reactions):

completely recovered
residual effects
reaction still present
died

patient receives treatment for reaction: yes; no
if yes, specify: _____

11. Investigator's overall evaluation taking into account expected spontaneous course of symptoms for individual patient.

Adverse reactions	Efficacy →	None	Poor	Fair	Good	Excellent
No adverse reactions	0				X	
Acceptable adverse reactions						
Unacceptable adverse reactions						

Comments, if any: _____

FIGURE 18

Start of treatment at onset of pain. DENTAL SURGERY FORM A

Diflunisal versus control

To be completed on day of surgery

Name or Initials: J.M.	Age: 17 yrs.	Sex: M F	Study nr: 38

Procedure: Removal of impacted tooth Impacted element: 18, 28, 38, 48.

Additional surgery, if any: none

Date of surgery: sept. 14 time ~~0 Hrs~~

Anesthesia given: general

Degree of trauma: mild ☐ moderate ☐ severe ☒

Exclusion criteria for participation in the study

Please check all items:

	YES	NO
__ Age below legal consent or over 70 years.	☐	☒
__ Confirmed pregnancy or a practical possibility of pregnancy	☐	☒
__ Hypersensitivity to salicylates or to the control medication	☐	☒
__ Current treatment with: systemic corticosteroid or anticoagulants.	☐	☒
__ Active peptic ulcer or g.i. hemorrhage.	☐	☒
__ Significant liver or kidney disease.	☐	☒
__ Hemopoietic disorders.	☐	☒

If none of these conditions applies to the patient, he or she may enter the study and receive test medication + instructions for use.

Start of treatment at onset of pain. DENTAL SURGERY FORM C

Diflunisal versus control

Investigator: Dr. M.L. McCUE

Name or Initials: J.M. Study nr: 38

MEDICATION (please record times in 0-24 hours)

Test medication:

first dose was taken at 1230 ....hour on day of surgery

second dose was taken at 1800 ....hour on day of surgery ☒ / day after surgery ☐

third dose was taken at ..... - ☐ - ☐

fourth dose was taken at ..... - ☐ - ☐

fifth dose was taken at ..... - ☐ - ☐

If not all doses were used, give reason: no further doses required for pain

Did patient take any other analgesic since surgery? No ☒ ; Yes

If yes, name of drug: Dose:

Time first dose was taken:

Did patient take strong alcoholic beverages? No X Yes If yes, specify number of glasses:

Did patient use drugs for other diseases No Yes XX If yes, specify: tetracycline 2 cap/day (name + dose)

FIGURE 19

DENTAL SURGERY — FORM B

Start of treatment at onset of pain.

Diflunisal versus control

Name of investigator: Dr. M.L. MCCUE

Name or initials: J.M. | Study nr: 38

CONTROL VISIT Evaluation on of day after surgery date: sept. 15 hour: 1200
Only to be filled in if patient took test medication.

1. PATIENTS EVALUATION

Parameters	At intake of first dose of test medication	At control visit	Description of rating scales on opposite page.
1. Pain	4	1	
11. Patient's opinion on treatment efficacy		4	

11. ADVERSE REACTIONS

None or specify below:	Maximal intensity	Seriousness	Drug relationship	Action taken if any
XXX				
Adverse reaction codes:	1 = mild 2 = moderate 3 = severe	1=not serious 2=serious	1=definitely not 2=probably not 3=possibly 4=probably 5=definitely	(e.g. dose reduction or discontinuation of test drug)

If adverse reaction was still present at control visit, give outcome if known (mandatory for serious reactions):

completely recovered
residual effects
reaction still present
died

patient receives treatment for reaction: yes; no
if yes, specify:

11. Investigator's overall evaluation taking into account expected spontaneous course of symptoms for individual patient.

Adverse reactions	Efficacy → None	Poor	Fair	Good	Excellent
No adverse reactions	0				X
Acceptable adverse reactions					
Unacceptable adverse reactions					

Comments, if any: patient was very satisfied with the medication

FIGURE 20

Start of treatment at onset of pain. DENTAL SURGERY FORM A

Diflunisal versus control

To be completed on day of surgery

Name or Initials: D.F.	Age: 19 yrs.	Sex: M F	Study nr: 39

Procedure: Removal of impacted teeth Impacted element: 38, 48.

Additional surgery, if any: 18

Date of surgery: sept. 14 time ___ a.m. Degree of trauma: mild ☐ moderate ☐ severe ☒

Anesthesia given: general

Exclusion criteria for participation in the study

Please check all items:

	YES	NO
__ Age below legal consent or over 70 years.	☐	☒
__ Confirmed pregnancy or a practical possibility of pregnancy	☐	☒
__ Hypersensitivity to salicylates or to the control medication	☐	☒
__ Current treatment with: systemic corticosteroid or anticoagulants.	☐	☒
__ Active peptic ulcer or g.i. hemorrhage.	☐	☒
__ Significant liver or kidney disease.	☐	☒
__ Hemopoietic disorders.	☐	☒

If none of these conditions applies to the patient, he or she may enter the study and receive test medication + instructions for use.

Start of treatment at onset of pain. DENTAL SURGERY FORM C

Diflunisal versus control Dr. M.L. McCue

Investigator:

Name or Initials: D.F.	Study nr: 39

MEDICATION (please record times in 0-24 hours)

Test medication:

first dose was taken at 1500 hour on day of surgery

second dose was taken at 1900 hour on day of surgery ☐ / day after surgery ☐

third dose was taken at 0300 - ☐ - ☒

fourth dose was taken at ..... - ☐ - ☐

fifth dose was taken at ..... - ☐ - ☐

If not all doses were used, give reason:

Did patient take any other analgesic since surgery? ☒ No ; Yes

If yes, name of drug: Dose:

Time first dose was taken:

Did patient take strong alcoholic beverages ☒ No Yes If yes, specify number of glasses:

Did patient use drugs for other diseases ☒ No Yes If yes, specify:

(name + dose)

FIGURE 21

DENTAL SURGERY FORM B

Start of treatment at onset of pain.

Diflunisal versus control

Name of investigator: Dr. M.L. McCUE

Name or initials: D.F. Study nr: 39

CONTROL VISIT Evaluation on of day after surgery date: sept. 15 hour: 1200

Only to be filled in if patient took test medication.

1. PATIENTS EVALUATION

Parameters	At intake of first dose of test medication	At control visit	Description of rating scales on opposite page.
1. Pain	2	0	
11. Patient's opinion on treatment efficacy	[illegible]	3	

11. ADVERSE REACTIONS

None xx or specify below:	Maximal intensity	Seriousness	Drug relationship	Action taken if any
Adverse reaction codes:	1 = mild 2 = moderate 3 = severe	1=not serious 2=serious	1=definitely not 2=probably not 3=possibly 4=probably 5=definitely	(e.g. dose reduction or discontinuation of test drug)

If adverse reaction was still present at control visit, give outcome if known (mandatory for serious reactions):

completely recovered
residual effects
reaction still present
died

patient receives treatment for reaction: yes; no
if yes, specify:

11. Investigator's overall evaluation taking into account expected spontaneous course of symptoms for individual patient.

Adverse reactions Efficacy →	None	Poor	Fair	Good	Excellent
No adverse reactions 0					x
Acceptable adverse reactions					
Unacceptable adverse reactions					

Comments, if any:

FIGURE 22

Start of treatment at onset of pain. DENTAL SURGERY FORM A

Diflunisal versus control

To be completed on day of surgery

Name or Initials: A.D.	Age: 28 yrs.	Sex: M / F	Study nr: 40

Procedure: Removal of impacted tooth Impacted element: 38, 48.

Additional surgery, if any: 18, 28.

Date of surgery: sept. 14 time am. Degree of trauma: mild ☐ moderate ☒ severe ☐

Anesthesia given: general

Exclusion criteria for participation in the study

Please check all items:

	YES	NO
__ Age below legal consent or over 70 years.	☐	☒
__ Confirmed pregnancy or a practical possibility of pregnancy	☐	☒
__ Hypersensitivity to salicylates or to the control medication	☐	☒
__ Current treatment with: systemic corticosteroid or anticoagulants.	☐	☒
__ Active peptic ulcer or g.i. hemorrhage.	☐	☒
__ Significant liver or kidney disease.	☐	☒
__ Hemopoietic disorders.	☐	☒

If none of these conditions applies to the patient, he or she may enter the study and receive test medication + instructions for use.

Start of treatment at onset of pain. DENTAL SURGERY FORM C

Diflunisal versus control

Investigator: Dr. M.L. McCUE

Name or initials: A.D. Study nr: 40

MEDICATION (please record times in 0-24 hours)

Test medication:

first dose was taken at 1645 hour on day of surgery

second dose was taken at 2045 hour on day of surgery ☒ */ day after surgery ☐

third dose was taken at 0045 - ☐ - ☒

fourth dose was taken at ..... - ☐ - ☐

fifth dose was taken at ..... - ☐ - ☐

If not all doses were used, give reason: did not require final dose

Did patient take any other analgesic since surgery? ☒ No : Yes

If yes, name of drug: Dose:

Time first dose was taken:

Did patient take strong alcoholic beverages ☒ No Yes If yes, specify number of glasses:

Did patient use drugs for other diseases No ☒ If yes, specify: flagyl (name + dose) 50 mg.

FIGURE 23

DENTAL SURGERY FORM B

Start of treatment at onset of pain.

Diflunisal versus control

Name of investigator: Dr. M.L. McCUE

Name or initials: A.D. Study nr: 40

CONTROL VISIT Evaluation on of day after surgery date: sept. 15 hour: 1300
Only to be filled in if patient took test medication.

1. PATIENTS EVALUATION

Parameters	At intake of first dose of test medication	At control visit	Description of rating scales on opposite page.
1. Pain	3	1	
11. Patient's opinion on treatment efficacy		3	

11. ADVERSE REACTIONS

XX None, or specify below:	Maximal intensity	Seriousness	Drug relationship	Action taken if any
Adverse reaction codes:	1 = mild 2 = moderate 3 = severe	1=not serious 2=serious	1=definitely not 2=probably not 3=possibly 4=probably 5=definitely	(e.g. dose reduction or discontinuation of test drug)

If adverse reaction was still present at control visit, give outcome if known (mandatory for serious reactions):

completely recovered
residual effects
reaction still present
died

patient receives treatment for reaction: yes; no
if yes, specify:

11. Investigator's overall evaluation taking into account expected spontaneous course of symptoms for individual patient.

Adverse reactions	Efficacy → None	Poor	Fair	Good	Excellent
No adverse reactions	0			X	
Acceptable adverse reactions					
Unacceptable adverse reactions					

Comments, if any: patient was satisified with the medication

FIGURE 24

Start of treatment at onset of pain. DENTAL SURGERY FORM A

Diflunisal versus control

To be completed on day of surgery

Name or Initials: D.M.	Age: 22 yrs.	Sex: F / M ✓	Study nr: 41

Procedure: Removal of impacted tooth Impacted element: 18 28, 38, 48, 13, 23.

Additional surgery, if any: none

Date of surgery: sept.14 time a.m. Degree of trauma: mild ☐ moderate ☐ severe ☒

Anesthesia given: general

Exclusion criteria for participation in the study

Please check all items:

	YES	NO
__ Age below legal consent or over 70 years.	☐	☒
__ Confirmed pregnancy or a practical possibility of pregnancy	☐	☒
__ Hypersensitivity to salicylates or to the control medication	☐	☒
__ Current treatment with: systemic corticosteroid or anticoagulants.	☐	☒
__ Active peptic ulcer or g.i. hemorrhage.	☐	☒
__ Significant liver or kidney disease.	☐	☒
__ Hemopoietic disorders.	☐	☒

If none of these conditions applies to the patient, he or she may enter the study and receive test medication + instructions for use.

Start of treatment at onset of pain. DENTAL SURGERY FORM C

Diflunisal versus control

Investigator: Dr. M.L. McCUE

Name or initials: D.M. Study nr: 41

MEDICATION (please record times in 0-24 hours)

Test medication:

first dose was taken at 1730 .....hour on day of surgery

second dose was taken at 2400 .....hour on day of surgery ☒ */ day after surgery ☐

third dose was taken at 0730 - ☐ - ☒

fourth dose was taken at ..... - ☐ - ☐

fifth dose was taken at ..... - ☐ - ☐

If not all doses were used, give reason:

Did patient take any other analgesic since surgery? No : ☒ Yes*

If yes, name of drug: 292 Dose: 1tab

Time first dose was taken: 1300 sept.15

Did patient take strong alcoholic beverages? ☒ No Yes If yes, specify number of glasses:

Did patient use drugs for other diseases ☒ No Yes If yes, specify:

(name + dose)

FIGURE 25

DENTAL SURGERY FORM B

Start of treatment at onset of pain.
Diflunisal versus control

Name of investigator: Dr. M.L. McCUE

Name or initials: D.M. Study nr: 41

CONTROL VISIT Evaluation on of day after surgery date: sept. 15 hour: 1400
Only to be filled in if patient took test medication.

1. PATIENTS EVALUATION

Parameters	At intake of first dose of test medication	At control visit	Description of rating scales on opposite page.
1. Pain	2	2	
11. Patient's opinion on treatment efficacy	[illegible]	2	

11. ADVERSE REACTIONS

None or specify below:	Maximal intensity	Seriousness	Drug relationship	Action taken if any
Adverse reaction codes:	1 = mild 2 = moderate 3 = severe	1=not serious 2=serious	1=definitely not 2=probably not 3=possibly 4=probably 5=definitely	(e.g. dose reduction or discontinuation of test drug)

If adverse reaction was still present at control visit, give outcome if known (mandatory for serious reactions):

completely recovered
residual effects
reaction still present
died

patient receives treatment for reaction: yes; no
if yes, specify: _____

11. Investigator's overall evaluation taking into account expected spontaneous course of symptoms for individual patient.

Adverse reactions	Efficacy → None	Poor	Fair	Good	Excellent
No adverse reactions	0		x		
Acceptable adverse reactions					
Unacceptable adverse reactions					

Comments, if any: pain was severe 24 hrs. following surgery
a 292 was required for pain

FIGURE 26

Start of treatment at onset of pain. DENTAL SURGERY FORM A

Diflunisal versus control

To be completed on day of surgery

Name or Initials: J.G.	Age: 20 yrs.	Sex: M F	Study nr: 42

Procedure: Removal of impacted tooth Impacted element: 18, 28, 38, 48.

Additional surgery, if any: none

Date of surgery: sept. 14 time ~~0715~~ Degree of trauma: mild ☐ moderate ☒ severe ☐

Anesthesia given: general

Exclusion criteria for participation in the study

Please check all items:

	YES	NO
__ Age below legal consent or over 70 years.	☐	☒
__ Confirmed pregnancy or a practical possibility of pregnancy	☐	☒
__ Hypersensitivity to salicylates or to the control medication	☐	☒
__ Current treatment with: systemic corticosteroid or anticoagulants.	☐	☒
__ Active peptic ulcer or g.i. hemorrhage.	☐	☒
__ Significant liver or kidney disease.	☐	☒
__ Hemopoietic disorders.	☐	☒

If none of these conditions applies to the patient, he or she may enter the study and receive test medication + instructions for use.

Start of treatment at onset of pain. DENTAL SURGERY FORM C

Diflunisal versus control

Investigator: Dr. M.L. McCUE

Name or initials: J.G. Study nr: 42

MEDICATION (please record times in 0-24 hours)

Test medication:

first dose was taken at 1630 hour on day of surgery

second dose was taken at 2030 hour on day of surgery ☒ */ day after surgery ☐

third dose was taken at 2330 - ☒ - ☐

fourth dose was taken at 0400 - ☐ - ☒

fifth dose was taken at ..... - ☐ - ☐

If not all doses were used, give reason:

Did patient take any other analgesic since surgery? ☒ No : Yes

If yes, name of drug: Dose:

Time first dose was taken:

Did patient take strong alcoholic beverages ☒ No Yes If yes, specify number of glasses:

Did patient use drugs for other diseases ☒ No Yes If yes, specify:

(name + dose)

FIGURE 27

DENTAL SURGERY FORM B

Start of treatment at onset of pain.

Diflunisal versus control

Name of investigator: Dr. M.L. McCUE

Name or initials: J.G. Study nr: 42

CONTROL VISIT Evaluation on of day after surgery date: sept. 15 hour: 1300
Only to be filled in if patient took test medication.

1. PATIENTS EVALUATION

Parameters	At intake of first dose of test medication	At control visit	Description of rating scales on opposite page.
1. Pain	3	0	
11. Patient's opinion on treatment efficacy		2	

11. ADVERSE REACTIONS

Non~~x~~ or specify below:	Maximal intensity	Seriousness	Drug relationship	Action taken if any
Adverse reaction codes:	1 = mild 2 = moderate 3 = severe	1=not serious 2=serious	1=definitely not 2=probably not 3=possibly 4=probably 5=definitely	(e.g. dose reduction or discontinuation of test drug)

If adverse reaction was still present at control visit, give outcome if known (mandatory for serious reactions):

completely recovered
residual effects
reaction still present
died

patient receives treatment for reaction: yes; no
if yes, specify: _____

11. Investigator's overall evaluation taking into account expected spontaneous course of symptoms for individual patient.

Adverse reactions	Efficacy → None	Poor	Fair	Good	Excellent
No adverse reactions	0		X		
Acceptable adverse reactions					
Unacceptable adverse reactions					

Comments, if any: the relief was too short lasting

FIGURE 28

Start of treatment at onset of pain. DENTAL SURGERY FORM A

Diflunisal versus control

To be completed on day of surgery

Name or Initials: L.P.	Age: 22 yrs.	Sex: F M	Study nr: 43

Procedure: Removal of impacted tooth Impacted element: 18, 28, 38, 48.

Additional surgery, if any: none

Date of surgery: Sept. 14 time a.m. Degree of trauma: mild ☐ moderate ☒ severe ☐

Anesthesia given: general

Exclusion criteria for participation in the study

Please check all items:

	YES	NO
__ Age below legal consent or over 70 years.	☐	☒
__ Confirmed pregnancy or a practical possibility of pregnancy	☐	☒
__ Hypersensitivity to salicylates or to the control medication	☐	☒
__ Current treatment with: systemic corticosteroid or anticoagulants.	☐	☒
__ Active peptic ulcer or g.i. hemorrhage.	☐	☒
__ Significant liver or kidney disease.	☐	☒
__ Hemopoietic disorders.	☐	☒

If none of these conditions applies to the patient, he or she may enter the study and receive test medication + instructions for use.

Start of treatment at onset of pain. DENTAL SURGERY FORM C

Dr. M.L. MOORE Diflunisal versus control

Investigator:

Name or initials: L.P. Study nr: 43

MEDICATION (please record times in 0-24 hours)

Test medication:

first dose was taken at 1830 hour on day of surgery

second dose was taken at 2230 hour on day of surgery ☒ */ day after surgery ☐

third dose was taken at 0230 - ☐ - ☒

fourth dose was taken at 1130 - ☐ - ☒

fifth dose was taken at ..... - ☐ - ☐

If not all doses were used, give reason:

Did patient take any other analgesic since surgery? ☒ No : Yes

If yes, name of drug: Dose:

Time first dose was taken:

Did patient take strong alcoholic beverages ☒ No Yes If yes, specify number of glasses:

Did patient use drugs for other diseases ☒ No Yes If yes, specify: (name + dose)

FIGURE 29

DENTAL SURGERY FORM B

Start of treatment at onset of pain.
Diflunisal versus control

Name of investigator: Dr. M.L. McCUE

Name or initials: L.P. Study nr: 43

CONTROL VISIT Evaluation on of day after surgery date: sept. 15 hour: 1300
Only to be filled in if patient took test medication.

1. PATIENTS EVALUATION

Parameters	At intake of first dose of test medication	At control visit	Description of rating scales on opposite page.
1. Pain	4	2	
11. Patient's opinion on treatment efficacy		2	

11. ADVERSE REACTIONS

None or specify below:	Maximal intensity	Seriousness	Drug relationship	Action taken if any
XXX				
Adverse reaction codes:	1 = mild 2 = moderate 3 = severe	1=not serious 2=serious	1=definitely not 2=probably not 3=possibly 4=probably 5=definitely	(e.g. dose reduction or discontinuation of test drug)

If adverse reaction was still present at control visit, give outcome if known (mandatory for serious reactions):

completely recovered
residual effects
reaction still present
died

patient receives treatment for reaction: yes; no
if yes, specify:

11. Investigator's overall evaluation taking into account expected spontaneous course of symptoms for individual patient.

Adverse reactions	Efficacy → None	Poor	Fair	Good	Excellent
No adverse reactions	0	X			
Acceptable adverse reactions					
Unacceptable adverse reactions					

Comments, if any: patient was not satisified with the medication

FIGURE 30

Start of treatment at onset of pain. DENTAL SURGERY FORM A

Diflunisal versus control

To be completed on day of surgery

Name or Initials: A.B.	Age: 20 yrs.	Sex: F M	Study nr: 44

Procedure: Removal of impacted tooth Impacted element: 18, 28, 38, 48.

Additional surgery, if any: none

Date of surgery: sept. 16 time ___ a.m. Degree of trauma: mild ☐ moderate ☒ severe ☐

Anesthesia given: general

Exclusion criteria for participation in the study

Please check all items:

	YES	NO
__ Age below legal consent or over 70 years.	☐	☒
__ Confirmed pregnancy or a practical possibility of pregnancy	☐	☒
__ Hypersensitivity to salicylates or to the control medication	☐	☒
__ Current treatment with: systemic corticosteroid or anticoagulants.	☐	☒
__ Active peptic ulcer or g.i. hemorrhage.	☐	☒
__ Significant liver or kidney disease.	☐	☒
__ Hemopoietic disorders.	☐	☒

If none of these conditions applies to the patient, he or she may enter the study and receive test medication + instructions for use.

Start of treatment at onset of pain. DENTAL SURGERY FORM C

Dr. M.L. McCUE Diflunisal versus control

Investigator: ___

Name or Initials: A.B. Study nr: 44

MEDICATION (please record times in 0-24 hours)

Test medication:

first dose was taken at 1130 hour on day of surgery

second dose was taken at 2000 hour on day of surgery ☐ */ day after surgery ☐

third dose was taken at ..... - ☐ - ☐

fourth dose was taken at ..... - ☐ - ☐

fifth dose was taken at ..... - ☐ - ☐

If not all doses were used, give reason: no further doses required for pain

Did patient take any other analgesic since surgery? ☒ No : ☐ Yes

If yes, name of drug: ___ Dose: ___

Time first dose was taken: ___

Did patient take strong alcoholic beverages ☒ No ☐ Yes If yes, specify number of glasses: ___

Did patient use drugs for other diseases ☒ No ☐ Yes If yes, specify: ___ (name + dose) ___

FIGURE 31

DENTAL SURGERY FORM B

Start of treatment at onset of pain.
Diflunisal versus control

Name of investigator: Dr. M.L. McCUE

Name or initials: A.B. Study nr: 44

CONTROL VISIT Evaluation on of day after surgery date: sept. 17 hour: 1200
Only to be filled in if patient took test medication.

1. PATIENTS EVALUATION

Parameters	At intake of first dose of test medication	At control visit	Description of rating scales on opposite page.
1. Pain	2	0	
11. Patient's opinion on treatment efficacy		4	

11. ADVERSE REACTIONS

None, or specify below:	Maximal intensity	Seriousness	Drug relationship	Action taken if any
a little nausea on first dose	1	1	3	none
Adverse reaction codes:	1 = mild 2 = moderate 3 = severe	1=not serious 2=serious	1=definitely not 2=probably not 3=possibly 4=probably 5=definitely	(e.g. dose reduction or discontinuation of test drug)

If adverse reaction was still present at control visit, give outcome if known (mandatory for serious reactions):

completely recovered
residual effects
reaction still present
died

patient receives treatment for reaction: yes; no
if yes, specify:

11. Investigator's overall evaluation taking into account expected spontaneous course of symptoms for individual patient.

Adverse reactions Efficacy →	None	Poor	Fair	Good	Excellenc
No adverse reactions					
Acceptable adverse reactions 1					x
Unacceptable adverse reactions					

Comments, if any: the nausea was short lived and did not occur with the second dose. The pain relief was rated as excellent

FIGURE 32

Start of treatment at onset of pain. DENTAL SURGERY FORM A

Diflunisal versus control

To be completed on day of surgery

Name or Initials: A.C.	Age: 22 yrs.	Sex: M / F ☒	Study nr: 45

Procedure: Removal of impacted tooth Impacted element: 18, 28, 38.

Additional surgery, if any: none

Date of surgery: ~~sept. 18~~ Time: ~~time~~ Degree of trauma: mild ☐ moderate ☒ severe ☐

Anesthesia given: general

Exclusion criteria for participation in the study

Please check all items:

	YES	NO
__ Age below legal consent or over 70 years.	☐	☒
__ Confirmed pregnancy or a practical possibility of pregnancy	☐	☒
__ Hypersensitivity to salicylates or to the control medication	☐	☒
__ Current treatment with: systemic corticosteroid or anticoagulants.	☐	☒
__ Active peptic ulcer or g.i. hemorrhage.	☐	☒
__ Significant liver or kidney disease.	☐	☒
__ Hemopoietic disorders.	☐	☒

If none of these conditions applies to the patient, he or she may enter the study and receive test medication + instructions for use.

Start of treatment at onset of pain. DENTAL SURGERY FORM C

Dr. M.L. McCUE Diflunisal versus control

Investigator:

Name or initials: A.C. Study nr: 45

MEDICATION (please record times in 0-24 hours)

Test medication:

first dose was taken at	1130 hour on day of surgery				
second dose was taken at	1600 hour on day of surgery	☐	*/ day after surgery	☐	
third dose was taken at	2300	-	☒	-	☐
fourth dose was taken at	0830	-	☐	-	☒
fifth dose was taken at	.....	-	☐	-	☐

If not all doses were used, give reasons:

Did patient take any other analgesic since surgery? ☒ No ; Yes

If yes, name of drug: Dose:

Time first dose was taken:

Did patient take strong alcoholic beverages ☒ No Yes If yes, specify number of glasses:

Did patient use drugs for other diseases ☒ No Yes If yes, specify: (name + dose)

FIGURE 33

DENTAL SURGERY FORM B

Start of treatment at onset of pain.

Diflunisal versus control

Name of investigator: Dr. M.L. McCUE

Name or initials: A.C. Study nr: 45

CONTROL VISIT Evaluation on of day after surgery date: sept. 17 hour: 1245
Only to be filled in if patient took test medication.

1. PATIENTS EVALUATION

Parameters	At intake of first dose of test medication	At control visit	Description of rating scales on opposite page.
I. Pain	2	0	
II. Patient's opinion on treatment efficacy	[illegible]	2	

11. ADVERSE REACTIONS

None xxx or specify below:	Maximal intensity	Seriousness	Drug relationship	Action taken if any
Adverse reaction codes:	1 = mild 2 = moderate 3 = severe	1=not serious 2=serious	1=definitely not 2=probably not 3=possibly 4=probably 5=definitely	(e.g. dose reduction or discontinuation of test drug)

If adverse reaction was still present at control visit, give outcome if known (mandatory for serious reactions):

completely recovered
residual effects
reaction still present
died

patient receives treatment for reaction: yes; no
if yes, specify: _____

11. Investigator's overall evaluation taking into account expected spontaneous course of symptoms for individual patient.

Adverse reactions	Efficacy →	None	Poor	Fair	Good	Excellent
No adverse reactions	0			X		
Acceptable adverse reactions						
Unacceptable adverse reactions						

Comments, if any: patient did not have much pain at any time but rated medication as only fair

FIGURE 34

Start of treatment at onset of pain. DENTAL SURGERY FORM A

Diflunisal versus control

To be completed on day of surgery

Name or Initials: E.C.	Age 22 yrs.	Sex: F ☒ M ☐	Study nr: 46

Procedure: Removal of impacted tooth Impacted element: 18, 38, 48.

Additional surgery, if any: none

Date of surgery: ~~sept. 16~~ time ~~a.m.~~ Degree of trauma: mild ☐ moderate ☒ severe ☐

Anesthesia given: general

Exclusion criteria for participation in the study

Please check all items:

	YES	NO
__ Age below legal consent or over 70 years.	☐	☒
__ Confirmed pregnancy or a practical possibility of pregnancy	☐	☒
__ Hypersensitivity to salicylates or to the control medication	☐	☒
__ Current treatment with: systemic corticosteroid or anticoagulants.	☐	☒
__ Active peptic ulcer or g.i. hemorrhage.	☐	☒
__ Significant liver or kidney disease.	☐	☒
__ Hemopoietic disorders.	☐	☒

If none of these conditions applies to the patient, he or she may enter the study and receive test medication + instructions for use.

Start of treatment at onset of pain. DENTAL SURGERY FORM C

Dr. [redacted] versus control

Investigator:

Name or initials: E.C. Study nr: 46

MEDICATION (please record times in 0-24 hours)

Test medication:

first dose was taken at 1400 ....hour on day of surgery

second dose was taken at 2000 ....hour on day of surgery ☒ */ day after surgery ☐

third dose was taken at ..... - ☐ - ☐

fourth dose was taken at ..... - ☐ - ☐

fifth dose was taken at ..... - ☐ - ☐

If not all doses were used, give reason: no further doses required pain was tolerable and had nausea with previous doses

Did patient take any other analgesic since surgery? ☒ No ; Yes

If yes, name of drug: Dose:

Time first dose was taken:

Did patient take strong alcoholic beverages: ☒ No Yes If yes, specify number of glasses:

Did patient use drugs for other diseases ☒ No Yes If yes, specify: (name + dose)

FIGURE 35

DENTAL SURGERY FORM B

Start of treatment at onset of pain.

Diflunisal versus control

Name of investigator: Dr. M.L. McCUE

Name or initials: E.C. Study nr: 46

CONTROL VISIT Evaluation on of day after surgery date: sept. 17 hour: 1200
Only to be filled in if patient took test medication.

1. PATIENTS EVALUATION

Parameters	At intake of first dose of test medication	At control visit	Description of rating scales on opposite page.
1. Pain	2	0	
11. Patient's opinion on treatment efficacy		2	

11. ADVERSE REACTIONS

None, or specify below:	Maximal intensity	Seriousness	Drug relationship	Action taken if any
nausea	1	1	3	disc. after 2nd dose
Adverse reaction codes:	1 = mild 2 = moderate 3 = severe	1=not serious 2=serious	1=definitely not 2=probably not 3=possibly 4=probably 5=definitely	(e.g. dose reduction or discontinuation of test drug)

If adverse reaction was still present at control visit, give outcome if known (mandatory for serious reactions):

completely recovered
residual effects
reaction still present
died

patient receives treatment for reaction: yes; no
if yes, specify:

11. Investigator's overall evaluation taking into account expected spontaneous course of symptoms for individual patient.

Adverse reactions Efficacy →	None	Poor	Fair	Good	Excellent
No adverse reactions					
Acceptable adverse reactions			x		
Unacceptable adverse reactions					

Comments, if any: caused patient nausea, was not too effective in relieving the pain

FIGURE 36

Start of treatment at onset of pain. DENTAL SURGERY FORM A

Diflunisal versus control

To be completed on day of surgery

Name or Initials: K.O.	Age: 17 yrs.	Sex: F (M / F)	Study nr: 47

Procedure: Removal of impacted teeth none Impacted element: 18, 28, 38, 48.

Additional surgery, if any: _____

Date of surgery: sept. 16 time ~~AM~~ Degree of trauma: mild ☐ moderate ☒ severe ☐

Anesthesia given: general

Exclusion criteria for participation in the study

Please check all items:

	YES	NO
__ Age below legal consent or over 70 years.	☐	☒
__ Confirmed pregnancy or a practical possibility of pregnancy	☐	☒
__ Hypersensitivity to salicylates or to the control medication	☐	☒
__ Current treatment with: systemic corticosteroid or anticoagulants.	☐	☒
__ Active peptic ulcer or g.i. hemorrhage.	☐	☒
__ Significant liver or kidney disease.	☐	☒
__ Hemopoietic disorders.	☐	☒

If none of these conditions applies to the patient, he or she may enter the study and receive test medication + instructions for use.

Start of treatment at onset of pain. DENTAL SURGERY FORM C

Diflunisal versus control

Investigator: Dr. M.L. MCCUE

Name or initials: K.O. Study nr: 47

MEDICATION (please record times in 0-24 hours)

Test medication:

first dose was taken at 2300 ..hour on day of surgery

second dose was taken at 0800 ....hour on day of surgery ☐ */ day after surgery ☒

third dose was taken at ..... = ☐ = ☐

fourth dose was taken at ..... = ☐ = ☐

fifth dose was taken at ..... = ☐ = ☐

If not all doses were used, give reason: _____

Did patient take any other analgesic since surgery? No ; ~~XX~~ Yes

If yes, name of drug: 222 Dose: 2tabs

Time first dose was taken: _____

Did patient take strong alcoholic beverages? No Yes If yes, specify number of glasses: _____

Did patient use drugs for other diseases ~~X~~ No Yes If yes, specify: _____

(name + dose) _____

FIGURE 37

DENTAL SURGERY FORM B

Start of treatment at onset of pain.

Diflunisal versus control

Name of investigator: Dr. M.L. MCCUE

Name or initials: K.O. Study nr: 47

CONTROL VISIT Evaluation on of day after surgery date: sept. 17 hour: 1200
Only to be filled in if patient took test medication.

1. PATIENTS EVALUATION

Parameters	At intake of first dose of test medication	At control visit	Description of rating scales on opposite page.
1. Pain			
11. Patient's opinion on treatment efficacy			

11. ADVERSE REACTIONS

None, or specify below:	Maximal intensity	Seriousness	Drug relationship	Action taken if any
Adverse reaction codes:	1 = mild 2 = moderate 3 = severe	1=not serious 2=serious	1=definitely not 2=probably not 3=possibly 4=probably 5=definitely	(e.g. dose reduction or discontinuation of test drug)

If adverse reaction was still present at control visit, give outcome if known (mandatory for serious reactions):

completely recovered
residual effects
reaction still present
died

patient receives treatment for reaction: yes; no
if yes, specify:

11. Investigator's overall evaluation taking into account expected spontaneous course of symptoms for individual patient.

Adverse reactions Efficacy →	None	Poor	Fair	Good	Excellenc
No adverse reactions					
Acceptable adverse reactions					
Unacceptable adverse reactions					

Comments, if any: patient was given another drug in error: for the first dose. Two test medications were given later and the results were good

FIGURE 38

Start of treatment at onset of pain. DENTAL SURGERY FORM A

Diflunisal versus control

To be completed on day of surgery

Name or Initials: J.H.	Age: 21 yrs.	Sex: M / F X	Study nr: 48

Procedure: Removal of impacted tooth Impacted element: 18, 38, 48.

Additional surgery, if any: none

Date of surgery: sept.16 time am* Degree of trauma: mild ☐ moderate X ☐ severe ☐

Anesthesia given: general

Exclusion criteria for participation in the study

Please check all items:

	YES	NO
__ Age below legal consent or over 70 years.	☐	X ☐
__ Confirmed pregnancy or a practical possibility of pregnancy	☐	X ☐
__ Hypersensitivity to salicylates or to the control medication	☐	X ☐
__ Current treatment with: systemic corticosteroid or anticoagulants.	☐	X ☐
__ Active peptic ulcer or g.i. hemorrhage.	☐	X ☐
__ Significant liver or kidney disease.	☐	X ☐
__ Hemopoietic disorders.	☐	X ☐

If none of these conditions applies to the patient, he or she may enter the study and receive test medication + instructions for use.

Start of treatment at onset of pain. DENTAL SURGERY FORM C

Diflunisal versus control

Investigator: ~~Dr.M.I. McGUE~~

Name or initials: J.H. Study nr: 48

MEDICATION (please record times in 0-24 hours)

Test medication:

first dose was taken at 1415 / 1830 ...hour on day of surgery

second dose was taken at .....hour on day of surgery ☐ X / day after surgery ☐

third dose was taken at	0150	-	☐	-	☒
fourth dose was taken at	1030	-	☐	-	☒
fifth dose was taken at	.....	-	☐	-	☐

If not all doses were used, give reason:

Did patient take any other analgesic since surgery? No : Yes

If yes, name of drug: Dose:

Time first dose was taken:

Did patient take strong alcoholic beverages No Yes If yes, specify number of glasses:

Did patient use drugs for other diseases No Yes If yes, specify: (name + dose)

FIGURE 39

DENTAL SURGERY — FORM B

Start of treatment at onset of pain.

Diflunisal versus control

Name of investigator: Dr. M.L. McCUE

Name or initials: J.H. | Study nr: 48

CONTROL VISIT Evaluation on of day after surgery date: sept. 17 hour: 1230
Only to be filled in if patient took test medication.

1. PATIENTS EVALUATION

Parameters	At intake of first dose of test medication	At control visit	Description of rating scales on opposite page.
1. Pain	4	1	
11. Patient's opinion on treatment efficacy	[illegible]	4	

11. ADVERSE REACTIONS

None or specify below:	Maximal intensity	Seriousness	Drug relationship	Action taken if any
Adverse reaction codes:	1 = mild 2 = moderate 3 = severe	1=not serious 2=serious	1=definitely not 2=probably not 3=possibly 4=probably 5=definitely	(e.g. dose reduction or discontinuation of test drug)

If adverse reaction was still present at control visit, give outcome if known (mandatory for serious reactions):

completely recovered
residual effects
reaction still present
died

patient receives treatment for reaction: yes; no
if yes, specify:

11. Investigator's overall evaluation taking into account expected spontaneous course of symptoms for individual patient.

Adverse reactions	Efficacy → None	Poor	Fair	Good	Excellent
No adverse reactions	0				X
Acceptable adverse reactions					
Unacceptable adverse reactions					

Comments, if any: patient was happy with the medication

FIGURE 40

Start of treatment at onset of pain. DENTAL SURGERY FORM A

Diflunisal versus control

To be completed on day of surgery

Name or Initials: R.G.	Age: 19 yrs.	Sex: M X F	Study nr: 49

Procedure: Removal of impacted tooth Impacted element: 18, 28, 38, 48.

Additional surgery, if any: none

Date of surgery: sept. 16 time RHo Degree of trauma: mild ☐ moderate ☒ severe ☐

Anesthesia given: general

Exclusion criteria for participation in the study

Please check all items:

	YES	NO
__ Age below legal consent or over 70 years.	☐	☒
__ Confirmed pregnancy or a practical possibility of pregnancy	☐	☒
__ Hypersensitivity to salicylates or to the control medication	☐	☒
__ Current treatment with: systemic corticosteroid or anticoagulants.	☐	☒
__ Active peptic ulcer or g.i. hemorrhage.	☐	☒
__ Significant liver or kidney disease.	☐	☒
__ Hemopoietic disorders.	☐	☒

If none of these conditions applies to the patient, he or she may enter the study and receive test medication + instructions for use.

Start of treatment at onset of pain. DENTAL SURGERY FORM C

Diflunisal versus control

Dr. M.L. McCue

Investigator:

Name or initials: R.G. Study nr: 49

MEDICATION (please record times in 0-24 hours)

Test medication:

first dose was taken at 1515 hour on day of surgery

second dose was taken at 2100 hour on day of surgery ☒ / day after surgery ☐

third dose was taken at 1015 - ☐ - ☒

fourth dose was taken at ..... - ☐ - ☐

fifth dose was taken at ..... - ☐ - ☐

If not all doses were used, give reason:

Did patient take any other analgesic since surgery? ☒ No ; Yes

If yes, name of drug: Dose:

Time first dose was taken:

Did patient take strong alcoholic beverages ☒ No Yes If yes, specify number of glasses:

Did patient use drugs for other diseases ☒ No Yes If yes, specify:

(name + dose)

FIGURE 41

DENTAL SURGERY — FORM B

Start of treatment at onset of pain.

Diflunisal versus control

Name of investigator: Dr. M.L. McCUE

Name or initials: R.G. Study nr: 49

CONTROL VISIT Evaluation on of day after surgery date: sept. 17 hour: 1230
Only to be filled in if patient took test medication.

1. PATIENTS EVALUATION

Parameters	At intake of first dose of test medication	At control visit	Description of rating scales on opposite page.
1. Pain	2	0	
11. Patient's opinion on treatment efficacy		4	

11. ADVERSE REACTIONS

None xxx or specify below:	Maximal intensity	Seriousness	Drug relationship	Action taken if any
Adverse reaction codes:	1 = mild 2 = moderate 3 = severe	1=not serious 2=serious	1=definitely not 2=probably not 3=possibly 4=probably 5=definitely	(e.g. dose reduction or discontinuation of test drug)

If adverse reaction was still present at control visit, give outcome if known (mandatory for serious reactions):

completely recovered
residual effects
reaction still present
died

patient receives treatment for reaction: yes; no
if yes, specify:

11. Investigator's overall evaluation taking into account expected spontaneous course of symptoms for individual patient.

Adverse reactions	Efficacy → None	Poor	Fair	Good	Excellent
No adverse reactions	0				x
Acceptable adverse reactions					
Unacceptable adverse reactions					

Comments, if any: patient was very happy with the medication

FIGURE 42

Start of treatment at onset of pain. DENTAL SURGERY FORM A

Diflunisal versus control

To be completed on day of surgery

Name or Initials: B.A.	Age: 23 yrs.	Sex: M / F	Study nr: 50

Procedure: Removal of impacted tooth Impacted element: 18, 28, 38, 48.

Additional surgery, if any: none

Date of surgery: sept. 16 time am. Degree of trauma: mild ☐ moderate ☒ severe ☐

Anesthesia given: general

Exclusion criteria for participation in the study

Please check all items:

	YES	NO
__ Age below legal consent or over 70 years.	☐	☒
__ Confirmed pregnancy or a practical possibility of pregnancy	☐	☒
__ Hypersensitivity to salicylates or to the control medication	☐	☒
__ Current treatment with: systemic corticosteroid or anticoagulants.	☐	☒
__ Active peptic ulcer or g.i. hemorrhage.	☐	☒
__ Significant liver or kidney disease.	☐	☒
__ Hemopoietic disorders.	☐	☒

If none of these conditions applies to the patient, he or she may enter the study and receive test medication + instructions for use.

Start of treatment at onset of pain. DENTAL SURGERY FORM C

Diflunisal versus control

Investigator: Dr. M.L. [illegible]

Name or initials: B.A. Study nr: 50

MEDICATION (please record times in 0-24 hours)

Test medication:

first dose was taken at 1530 hour on day of surgery

second dose was taken at 1930 hour on day of surgery ☒ / day after surgery ☐

third dose was taken at 2330 - ☐ - ☐

fourth dose was taken at ..... - ☐ - ☐

fifth dose was taken at ..... - ☐ - ☐

If not all doses were used, give reason: the final dose was not required

Did patient take any other analgesic since surgery? ☒ No ; Yes

If yes, name of drug: Dose:

Time first dose was taken:

Did patient take strong alcoholic beverages: ☒ No Yes If yes, specify number of glasses:

Did patient use drugs for other diseases ☒ No Yes If yes, specify: (name + dose)

FIGURE 43

DENTAL SURGERY FORM B

Start of treatment at onset of pain.

Diflunisal versus control

Name of investigator: Dr.M.L. McCUE

Name or initials: B.A. Study nr: 50

CONTROL VISIT Evaluation on of day after surgery date: sept. 17 hour: 1245
Only to be filled in if patient took test medication.

1. PATIENTS EVALUATION

Parameters	At intake of first dose of test medication	At control visit	Description of rating scales on opposite page.
1. Pain	3	0	
11. Patient's opinion on treatment efficacy		4	

11. ADVERSE REACTIONS

None or specify below:	Maximal intensity	Seriousness	Drug relationship	Action taken if any
Adverse reaction codes:	1 = mild 2 = moderate 3 = severe	1=not serious 2=serious	1=definitely not 2=probably not 3=possibly 4=probably 5=definitely	(e.g. dose reduction or discontinuation of test drug)

If adverse reaction was still present at control visit, give outcome if known (mandatory for serious reactions):

completely recovered
residual effects
reaction still present
died

patient receives treatment for reaction: yes; no
if yes, specify:

11. Investigator's overall evaluation taking into account expected spontaneous course of symptoms for individual patient.

Adverse reactions	Efficacy → None	Poor	Fair	Good	Excellent
No adverse reactions	0				x
Acceptable adverse reactions					
Unacceptable adverse reactions					

Comments, if any: patient was happy with the medication

FIGURE 44

Start of treatment at onset of pain. DENTAL SURGERY FORM A

Diflunisal versus control

To be completed on day of surgery

Name or Initials: C.' .	Age: 20 yrs.	Sex: F M	Study nr: 51

Procedure: Removal of impacted tooth Impacted element: 18, 28, 38, 48 and supernummery

Additional surgery, if any: none

Date of surgery: sept.16 time am. Degree of trauma: mild ☐ moderate ☐ severe X ☐

Anesthesia given: general

Exclusion criteria for participation in the study

Please check all items:

	YES	NO
__ Age below legal consent or over 70 years.	☐	X
__ Confirmed pregnancy or a practical possibility of pregnancy	☐	X
__ Hypersensitivity to salicylates or to the control medication	☐	X
__ Current treatment with: systemic corticosteroid or anticoagulants.	☐	X
__ Active peptic ulcer or g.i. hemorrhage.	☐	X
__ Significant liver or kidney disease.	☐	X
__ Hemopoietic disorders.	☐	X

If none of these conditions applies to the patient, he or she may enter the study and receive test medication + instructions for use.

Start of treatment at onset of pain. DENTAL SURGERY FORM C

Diflunisal versus control

Investigator: Dr. [redacted] .L. McCUE

Name or initials: C.' . Study nr: 51

MEDICATION (please record times in 0-24 hours)

Test medication:

first dose was taken at 1730 hour on day of surgery

second dose was taken at 2400 hour on day of surgery X ☐ */ day after surgery ☐

third dose was taken at 0930 - ☐ - X ☐

fourth dose was taken at ..... - ☐ - ☐

fifth dose was taken at ..... - ☐ - ☐

If not all doses were used, give reason:

Did patient take any other analgesic since surgery? X No ; Yes

If yes, name of drug: Dose:

Time first dose was taken:

Did patient take strong alcoholic beverages X No Yes If yes, specify number of glasses:

Did patient use drugs for other diseases X No Yes If yes, specify:

(name + dose)

FIGURE 45

DENTAL SURGERY FORM B

Start of treatment at onset of pain.
Diflunisal versus control

Name of investigator: DR. M.L. MCCUE

Name or initials: C.A. Study nr: 51

CONTROL VISIT Evaluation on of day after surgery date: sept 17 hour: 1300
Only to be filled in if patient took test medication.

1. PATIENTS EVALUATION

Parameters	At intake of first dose of test medication	At control visit	Description of rating scales on opposite page.
1. Pain	1	1	
11. Patient's opinion on treatment efficacy		3	

11. ADVERSE REACTIONS

None, or specify below:	Maximal intensity	Seriousness	Drug relationship	Action taken if any
nausea and drowsiness	1	1	3	none
Adverse reaction codes:	1 = mild 2 = moderate 3 = severe	1=not serious 2=serious	1=definitely not 2=probably not 3=possibly 4=probably 5=definitely	(e.g. dose reduction or discontinuation of test drug)

If adverse reaction was still present at control visit, give outcome if known (mandatory for serious reactions):

completely recovered
residual effects
reaction still present
died

patient receives treatment for reaction: yes; no
if yes, specify:

11. Investigator's overall evaluation taking into account expected spontaneous course of symptoms for individual patient.

Adverse reactions Efficacy →	None	Poor	Fair	Good	Excellent
No adverse reactions					
Acceptable adverse reactions 1				X	
Unacceptable adverse reactions					

Comments, if any: nausea and drowsiness after the second dose

FIGURE 46

Start of treatment at onset of pain. DENTAL SURGERY FORM A

Diflunisal versus control

To be completed on day of surgery

Name or Initials: J.T.	Age: 30 yrs.	Sex: M F	Study nr: 52

Procedure: Removal of impacted tooth Impacted element: 48

Additional surgery, if any: none

Date of surgery: ~~sept. 21~~ time ~~a.m.~~ Degree of trauma: mild ☐ moderate ☒ severe ☐

Anesthesia given: local anaesth. and I.V. sedation

Exclusion criteria for participation in the study

Please check all items:

	YES	NO
__ Age below legal consent or over 70 years.	☐	☒
__ Confirmed pregnancy or a practical possibility of pregnancy	☐	☒
__ Hypersensitivity to salicylates or to the control medication	☐	☒
__ Current treatment with: systemic corticosteroid or anticoagulants.	☐	☒
__ Active peptic ulcer or g.i. hemorrhage.	☐	☒
__ Significant liver or kidney disease.	☐	☒
__ Hemopoietic disorders.	☐	☒

If none of these conditions applies to the patient, he or she may enter the study and receive test medication + instructions for use.

Start of treatment at onset of pain. DENTAL SURGERY FORM C

Diflunisal versus control

Investigator: Dr. A. L. McCUE

Name or initials: J.T. Study nr: 52

MEDICATION (please record times in 0-24 hours)

Test medication:

first dose was taken at 1100 ....hour on day of surgery

second dose was taken at 1430 .....hour on day of surgery ☐ °/ day after surgery ☐

third dose was taken at 1830 ..... - ☒ - ☐

fourth dose was taken at 0730 - ☐ - ☒

fifth dose was taken at ..... - ☐ - ☐

If not all doses were used, give reason:

Did patient take any other analgesic since surgery? ~~No~~ ; Yes

If yes, name of drug: Dose:

Time first dose was taken:

Did patient take strong alcoholic beverages ~~No~~ Yes If yes, specify number of glasses:

Did patient use drugs for other diseases ~~No~~ Yes If yes, specify:

(name + dose)

FIGURE 47

DENTAL SURGERY FORM B

Start of treatment at onset of pain.

Diflunisal versus control

Name of investigator: Dr. M.L. McCUE

Name or initials: J.T. Study nr: 52

CONTROL VISIT Evaluation on of day after surgery date: sept. 23 hour: 1400
Only to be filled in if patient took test medication.

1. PATIENTS EVALUATION

Parameters	At intake of first dose of test medication	At control visit	Description of rating scales on opposite page.
1. Pain	1	1	
11. Patient's opinion on treatment efficacy		3	

11. ADVERSE REACTIONS

None, or specify below: XX	Maximal intensity	Seriousness	Drug relationship	Action taken if any
Adverse reaction codes:	1 = mild 2 = moderate 3 = severe	1=not serious 2=serious	1=definitely not 2=probably not 3=possibly 4=probably 5=definitely	(e.g. dose reduction or discontinuation of test drug)

If adverse reaction was still present at control visit, give outcome if known (mandatory for serious reactions):

completely recovered
residual effects
reaction still present
died

patient receives treatment for reaction: yes; no
if yes, specify:

11. Investigator's overall evaluation taking into account expected spontaneous course of symptoms for individual patient.

Adverse reactions Efficacy →	None	Poor	Fair	Good	Excellent
No adverse reactions	0			x	
Acceptable adverse reactions					
Unacceptable adverse reactions					

Comments, if any:

FIGURE 48

Start of treatment at onset of pain. DENTAL SURGERY FORM A

Diflunisal versus control

To be completed on day of surgery

Name or Initials: D.W.	Age: 30 yrs.	Sex: M / F	Study nr: 53

Procedure: Removal of impacted tooth Impacted element: 38

Additional surgery, if any: none

Date of surgery: sept. 21 time am. Degree of trauma: mild ☐ moderate ☒ severe ☐

Anesthesia given: local anaesth. and I.V. sedation

Exclusion criteria for participation in the study

Please check all items:

	YES	NO
__ Age below legal consent or over 70 years.	☐	☒
__ Confirmed pregnancy or a practical possibility of pregnancy	☐	☒
__ Hypersensitivity to salicylates or to the control medication	☐	☒
__ Current treatment with: systemic corticosteroid or anticoagulants.	☐	☒
__ Active peptic ulcer or g.i. hemorrhage.	☐	☒
__ Significant liver or kidney disease.	☐	☒
__ Hemopoietic disorders.	☐	☒

If none of these conditions applies to the patient, he or she may enter the study and receive test medication + instructions for use.

Start of treatment at onset of pain. DENTAL SURGERY FORM C

Diflunisal versus control

Investigator: Dr. ..L. McCUE

Name or initials: D.W. Study nr: 53

MEDICATION (please record times in 0-24 hours)

Test medication:

first dose was taken at .....hour on day of surgery

second dose was taken at .....hour on day of surgery ☐ */ day after surgery ☐

third dose was taken at ..... - ☐ - ☐

fourth dose was taken at ..... - ☐ - ☐

fifth dose was taken at ..... - ☐ - ☐

If not all doses were used, give reason:

Did patient take any other analgesic since surgery? No ; Yes

If yes, name of drug: Dose:

Time first dose was taken:

Did patient take strong alcoholic beverages No Yes If yes, specify number of glasses:

Did patient use drugs for other diseases No Yes If yes, specify:

(name + dose)

FIGURE 49

DENTAL SURGERY FORM B

Start of treatment at onset of pain.

Diflunisal versus control

Name of investigator: Dr. M.L. McCUE

Name or initials: D.J. Study nr: 53

CONTROL VISIT Evaluation on of day after surgery date: _____ hour: _____
Only to be filled in if patient took test medication.

1. PATIENTS EVALUATION

Parameters	At intake of first dose of test medication	At control visit	Description of rating scales on opposite page.
1. Pain			
11. Patient's opinion on treatment efficacy			

11. ADVERSE REACTIONS

None, or specify below:	Maximal intensity	Seriousness	Drug relationship	Action taken if any
Adverse reaction codes:	1 = mild 2 = moderate 3 = severe	1=not serious 2=serious	1=definitely not 2=probably not 3=possibly 4=probably 5=definitely	(e.g. dose reduction or discontinuation of test drug)

If adverse reaction was still present at control visit, give outcome if known (mandatory for serious reactions):

completely recovered
residual effects
reaction still present
died

patient receives treatment for reaction: yes; no
if yes, specify: _____

11. Investigator's overall evaluation taking into account expected spontaneous course of symptoms for individual patient.

Adverse reactions Efficacy →	None	Poor	Fair	Good	Excellent
No adverse reactions					
Acceptable adverse reactions					
Unacceptable adverse reactions					

Comments, if any: patient could not be contacted

FIGURE 50

Start of treatment at onset of pain. DENTAL SURGERY FORM A

Diflunisal versus control

To be completed on day of surgery

Name or Initials: J.M.	Age: 26 yrs.	Sex: F M	Study nr: 54

Procedure: Removal of impacted tooth Impacted element: 18

Additional surgery, if any: none

Date of surgery: sept. 24 Time: am. Degree of trauma: mild ☐
moderate ☒
severe ☐

Anesthesia given: local anaesth. and I.V. sedation

Exclusion criteria for participation in the study

Please check all items:

	YES	NO
__ Age below legal consent or over 70 years.	☐	☒
__ Confirmed pregnancy or a practical possibility of pregnancy	☐	☒
__ Hypersensitivity to salicylates or to the control medication	☐	☒
__ Current treatment with: systemic corticosteroid or anticoagulants.	☐	☒
__ Active peptic ulcer or g.i. hemorrhage.	☐	☒
__ Significant liver or kidney disease.	☐	☒
__ Hemopoietic disorders.	☐	☒

If none of these conditions applies to the patient, he or she may enter the study and receive test medication + instructions for use.

Start of treatment at onset of pain. DENTAL SURGERY FORM C

Diflunisal versus control

Investigator: Dr. M.L. McCUE

Name or initials: J.M. Study nr: 54

MEDICATION (please record times in 0-24 hours)

Test medication:

first dose was taken at .....hour on day of surgery

second dose was taken at .....hour on day of surgery ☐ */ day after surgery ☐

third dose was taken at ..... - ☐ - ☐

fourth dose was taken at ..... - ☐ - ☐

fifth dose was taken at ..... - ☐ - ☐

If not all doses were used, give reason: no medication was required for pain

Did patient take any other analgesic since surgery? No X ; Yes

If yes, name of drug: Dose:

Time first dose was taken:

Did patient take strong alcoholic beverages? No Yes If yes, specify number of glasses:

Did patient use drugs for other diseases No Yes If yes, specify:
(name + dose)

FIGURE 51

DENTAL SURGERY FORM B

Start of treatment at onset of pain.

Diflunisal versus control

Name of investigator: Dr. M.L. McCUE

Name or initials: J.M. Study nr: 54

CONTROL VISIT Evaluation on of day after surgery date: sept. 22 hour: 1200
Only to be filled in if patient took test medication.

I. PATIENTS EVALUATION

Parameters	At intake of first dose of test medication	At control visit	Description of rating scales on opposite page.
1. Pain			
11. Patient's opinion on treatment efficacy			

II. ADVERSE REACTIONS

None, or specify below:	Maximal intensity	Seriousness	Drug relationship	Action taken if any
Adverse reaction codes:	1 = mild 2 = moderate 3 = severe	1=not serious 2=serious	1=definitely not 2=probably not 3=possibly 4=probably 5=definitely	(e.g. dose reduction or discontinuation of test drug)

If adverse reaction was still present at control visit, give outcome if known (mandatory for serious reactions):

completely recovered
residual effects
reaction still present
died

patient receives treatment for reaction: yes; no
if yes, specify:

II. Investigator's overall evaluation taking into account expected spontaneous course of symptoms for individual patient.

Adverse reactions Efficacy →	None	Poor	Fair	Good	Excellent
No adverse reactions					
Acceptable adverse reactions					
Unacceptable adverse reactions					

Comments, if any: patient did not require any medication

FIGURE 52

Start of treatment at onset of pain. DENTAL SURGERY FORM A

Diflunisal versus control

To be completed on day of surgery

Name or Initials: S.M.	Age: 19 yrs.	Sex: F M	Study nr: 55

Procedure: Removal of impacted tooth Impacted element: 18, 28, 38, 48.

Additional surgery, if any: none

Date of surgery: sept. 23 time 4 P.M. Degree of trauma: mild ☐ moderate ☒ severe ☐

Anesthesia given: general

Exclusion criteria for participation in the study

Please check all items:

	YES	NO
__ Age below legal consent or over 70 years.	☐	☒
__ Confirmed pregnancy or a practical possibility of pregnancy	☐	☒
__ Hypersensitivity to salicylates or to the control medication	☐	☒
__ Current treatment with: systemic corticosteroid or anticoagulants.	☐	☒
__ Active peptic ulcer or g.i. hemorrhage.	☐	☒
__ Significant liver or kidney disease.	☐	☒
__ Hemopoietic disorders.	☐	☒

If none of these conditions applies to the patient, he or she may enter the study and receive test medication + instructions for use.

Start of treatment at onset of pain. DENTAL SURGERY FORM C

Diflunisal versus control

Dr. M.L. McCUE

Investigator:

Name or initials: S.M. Study nr: 55

MEDICATION (please record times in 0-24 hours)

Test medication:

first dose was taken at 1100 hour on day of surgery

second dose was taken at 1800 hour on day of surgery ☒ */ day after surgery ☐

third dose was taken at 1100 " ☐ " ☒

fourth dose was taken at ..... " ☐ " ☐

fifth dose was taken at ..... " ☐ " ☐

If not all doses were used, give reason:

Did patient take any other analgesic since surgery? No X ; Yes

If yes, name of drug: Dose:

Time first dose was taken:

Did patient take strong alcoholic beverages No X Yes If yes, specify number of glasses:

Did patient use drugs for other diseases No X Yes If yes, specify:

(name + dose)

FIGURE 53

DENTAL SURGERY FORM B

Start of treatment at onset of pain.

Diflunisal versus control

Name of investigator: Dr. M.L. McCUE

Name or initials: S.M.	Study nr: 55

CONTROL VISIT Evaluation on of day after surgery date: sept. 24 hour: 1600
Only to be filled in if patient took test medication.

1. PATIENTS EVALUATION

Parameters	At intake of first dose of test medication	At control visit	Description of rating scales on opposite page.
1. Pain	3	1	
11. Patient's opinion on treatment efficacy		3	

11. ADVERSE REACTIONS

XX None, or specify below:	Maximal intensity	Seriousness	Drug relationship	Action taken if any
Adverse reaction codes:	1 = mild 2 = moderate 3 = severe	1=not serious 2=serious	1=definitely not 2=probably not 3=possibly 4=probably 5=definitely	(e.g. dose reduction or discontinuation of test drug)

If adverse reaction was still present at control visit, give outcome if known (mandatory for serious reactions):

completely recovered
residual effects
reaction still present
died

patient receives treatment for reaction: yes; no
if yes, specify:

11. Investigator's overall evaluation taking into account expected spontaneous course of symptoms for individual patient.

Adverse reactions Efficacy →	None	Poor	Fair	Good	Excellent
No adverse reactions	0			x	
Acceptable adverse reactions					
Unacceptable adverse reactions					

Comments, if any: patient was pleased with the medication but felt the onset of relief was slow

FIGURE 54

Start of treatment at onset of pain. DENTAL SURGERY FORM A

Diflunisal versus control

To be completed on day of surgery

Name or Initials: J.C.	Age: 23 yrs.	Sex: F M Y	Study nr: 56

Procedure: Removal of impacted tooth Impacted element: 18, 28, 38, 48.

Additional surgery, if any: none

Date of surgery: sept. 23 time 2 p.m. Degree of trauma: mild ☐ moderate ☒ severe ☐

Anesthesia given: general

Exclusion criteria for participation in the study

Please check all items:

	YES	NO
__ Age below legal consent or over 70 years.	☐	☒
__ Confirmed pregnancy or a practical possibility of pregnancy	☐	☒
__ Hypersensitivity to salicylates or to the control medication	☐	☒
__ Current treatment with: systemic corticosteroid or anticoagulants.	☐	☒
__ Active peptic ulcer or g.i. hemorrhage.	☐	☒
__ Significant liver or kidney disease.	☐	☒
__ Hemopoietic disorders.	☐	☒

If none of these conditions applies to the patient, he or she may enter the study and receive test medication + instructions for use.

Start of treatment at onset of pain. DENTAL SURGERY FORM C

Diflunisal versus control

Investigator: DR. M.L. McCUE

Name or initials: J.C. Study nr: 56

MEDICATION (please record times in 0-24 hours)

Test medication:

first dose was taken at 1015 hour on day of surgery

second dose was taken at 1430 hour on day of surgery ☐ / day after surgery ☐

third dose was taken at 1815 " ☒ " ☐

fourth dose was taken at ..... " ☐ " ☐

fifth dose was taken at ..... " ☐ " ☐

If not all doses were used, give reason: substituted 292 for the final dose

Did patient take any other analgesic since surgery? No ; Yes

If yes, name of drug: 292 Dose: 1tab.

Time first dose was taken: 0800 sept.24

Did patient take strong alcoholic beverages? No Yes If yes, specify number of glasses:

Did patient use drugs for other diseases No Yes If yes, specify:

(name + dose)

FIGURE 55

DENTAL SURGERY FORM B

Start of treatment at onset of pain.

Diflunisal versus control

Name of investigator: Dr. M.L. McCUE

Name or initials: J.C. Study nr: 56

CONTROL VISIT Evaluation on of day after surgery date: sept. 24 hour: 1600
Only to be filled in if patient took test medication.

1. PATIENTS EVALUATION

Parameters	At intake of first dose of test medication	At control visit	Description of rating scales on opposite page.
1. Pain	4	2	
11. Patient's opinion on treatment efficacy		2	

11. ADVERSE REACTIONS

XX None, or specify below:	Maximal intensity	Seriousness	Drug relationship	Action taken if any
Adverse reaction codes:	1 = mild 2 = moderate 3 = severe	1=not serious 2=serious	1=definitely not 2=probably not 3=possibly 4=probably 5=definitely	(e.g. dose reduction or discontinuation of test drug)

If adverse reaction was still present at control visit, give outcome if known (mandatory for serious reactions):

completely recovered
residual effects
reaction still present
died

patient receives treatment for reaction: yes; no
if yes, specify:

11. Investigator's overall evaluation taking into account expected spontaneous course of symptoms for individual patient.

Adverse reactions	Efficacy → None	Poor	Fair	Good	Excellent
No adverse reactions		X			
Acceptable adverse reactions					
Unacceptable adverse reactions					

Comments, if any: patient required for the final dose a 292

FIGURE 56

Start of treatment at onset of pain. DENTAL SURGERY FORM A

Diflunisal versus control

To be completed on day of surgery

Name or Initials: G.G.	Age: 18 yrs.	Sex: M F	Study nr: 57

Procedure: Removal of impacted tooth Impacted element: 18, 28, 38, 48.

Additional surgery, if any: none

Date of surgery: sept. 23 time a.m. Degree of trauma: mild ☐ moderate ☒ severe ☐

Anesthesia given: general

Exclusion criteria for participation in the study

Please check all items:

	YES	NO
__ Age below legal consent or over 70 years.	☐	X ☐
__ Confirmed pregnancy or a practical possibility of pregnancy	☐	☒
__ Hypersensitivity to salicylates or to the control medication	☐	X ☐
__ Current treatment with: systemic corticosteroid or anticoagulants.	☐	☒
__ Active peptic ulcer or g.i. hemorrhage.	☐	☒
__ Significant liver or kidney disease.	☐	☒
__ Hemopoietic disorders.	☐	☒

If none of these conditions applies to the patient, he or she may enter the study and receive test medication + instructions for use.

Start of treatment at onset of pain. DENTAL SURGERY FORM C

Diflunisal versus control

Investigator: Dr. M.L. MCCUE

Name or initials: G.G. Study nr: 57

MEDICATION (please record times in 0-24 hours)

Test medication:

first dose was taken at	1145 hour on day of surgery				
second dose was taken at	1630 hour on day of surgery ☒ / day after surgery ☐				
third dose was taken at	2030	-	☒	-	☐
fourth dose was taken at	0430	-	☐	-	☒
fifth dose was taken at	.....	-	☐	-	☐

If not all doses were used, give reason:

Did patient take any other analgesic since surgery? No : Yes

If yes, name of drug: 292 Dose: 1 tab

Time first dose was taken: sept. 24 0800 hrs.

Did patient take strong alcoholic beverages No Yes If yes, specify number of glasses:

Did patient use drugs for other diseases No Yes If yes, specify: (name + dose)

FIGURE 57

DENTAL SURGERY FORM B

Start of treatment at onset of pain.

Diflunisal versus control

Name of investigator: Dr. M.L. McCUE

Name or initials: G.G. Study nr: 57

CONTROL VISIT Evaluation on of day after surgery date: sept. 24 hour: 1600
Only to be filled in if patient took test medication.

1. PATIENTS EVALUATION

Parameters	At intake of first dose of test medication	At control visit	Description of rating scales on opposite page.
1. Pain	3	1	
11. Patient's opinion on treatment efficacy	[illegible]	2	

11. ADVERSE REACTIONS

None or specify below:	Maximal intensity	Seriousness	Drug relationship	Action taken if any
Adverse reaction codes:	1 = mild 2 = moderate 3 = severe	1=not serious 2=serious	1=definitely not 2=probably not 3=possibly 4=probably 5=definitely	(e.g. dose reduction or discontinuation of test drug)

If adverse reaction was still present at control visit, give outcome if known (mandatory for serious reactions):

completely recovered
residual effects
reaction still present
died

patient receives treatment for reaction: yes; no
if yes, specify:

11. Investigator's overall evaluation taking into account expected spontaneous course of symptoms for individual patient.

Adverse reactions	Efficacy →	None	Poor	Fair	Good	Excellent
No adverse reactions	0			x		
Acceptable adverse reactions						
Unacceptable adverse reactions						

Comments, if any: patient finished medication but found that 292 much superior

FIGURE 58

Start of treatment at onset of pain. DENTAL SURGERY FORM A

Diflunisal versus control

To be completed on day of surgery

Name or Initials: M.S.	Age: 18 yrs.	Sex: F M	Study nr: 58

Procedure: Removal of impacted tooth Impacted element: 18, 28, 38, 48.

Additional surgery, if any: none

Date of surgery: sept. 24 a.m. Degree of trauma: mild ☐ moderate ☒ severe ☐

Anesthesia given: general

Exclusion criteria for participation in the study

Please check all items:

	YES	NO
__ Age below legal consent or over 70 years.	☐	☒
__ Confirmed pregnancy or a practical possibility of pregnancy	☐	☒
__ Hypersensitivity to salicylates or to the control medication	☐	☒
__ Current treatment with: systemic corticosteroid or anticoagulants.	☐	☒
__ Active peptic ulcer or g.i. hemorrhage.	☐	☒
__ Significant liver or kidney disease.	☐	☒
__ Hemopoietic disorders.	☐	☒

If none of these conditions applies to the patient, he or she may enter the study and receive test medication + instructions for use.

Start of treatment at onset of pain. DENTAL SURGERY FORM C

Diflunisal versus control Dr. M.L. McCUE

Investigator:

Name or initials: M.S. Study nr: 58

MEDICATION (please record times in 0-24 hours)

Test medication:

first dose was taken at 1030 hour on day of surgery

second dose was taken at .....hour on day of surgery ☐ */ day after surgery ☐

third dose was taken at ..... - ☐ - ☐

fourth dose was taken at ..... - ☐ - ☐

fifth dose was taken at ..... - ☐ - ☐

If not all doses were used, give reason: patient became nauseous after first dose and discontinued study

Did patient take any other analgesic since surgery? No X ; Yes

If yes, name of drug: Dose:

Time first dose was taken:

Did patient take strong alcoholic beverages No X Yes If yes, specify number of glasses:

Did patient use drugs for other diseases No X Yes If yes, specify: (name + dose)

FIGURE 59

DENTAL SURGERY FORM B

Start of treatment at onset of pain.

Diflunisal versus control

Name of investigator: Dr. M.L. McCUE

Name or initials: M.S. Study nr: 58

CONTROL VISIT Evaluation on of day after surgery date: sept. 24 hour: 1800
Only to be filled in if patient took test medication.

1. PATIENTS EVALUATION

Parameters	At intake of first dose of test medication	At control visit	Description of rating scales on opposite page.
1. Pain	2		
11. Patient's opinion on treatment efficacy	[illegible]	?	

11. ADVERSE REACTIONS

None, or specify below:	Maximal intensity	Seriousness	Drug relationship	Action taken if any
nausea	1	1	3	disc. drug
Adverse reaction codes:	1 = mild 2 = moderate 3 = severe	1=not serious 2=serious	1=definitely not 2=probably not 3=possibly 4=probably 5=definitely	(e.g. dose reduction or discontinuation of test drug)

If adverse reaction was still present at control visit, give outcome if known (mandatory for serious reactions):

completely recovered
residual effects
reaction still present
died

patient receives treatment for reaction: yes; no
if yes, specify: _____

11. Investigator's overall evaluation taking into account expected spontaneous course of symptoms for individual patient.

Adverse reactions Efficacy →	None	Poor	Fair	Good	Excellenc
No adverse reactions					
Acceptable adverse reactions	1				
Unacceptable adverse reactions					

Comments, if any: patient experienced nausea after first dose and discontinued study

FIGURE 60

Start of treatment at onset of pain. DENTAL SURGERY FORM A

Diflunisal versus control

To be completed on day of surgery

Name or Initials: G.M.	Age: 34 yrs.	Sex: F M	Study nr: 59

Procedure: Removal of impacted tooth Impacted element: 18, 38, 48.

Additional surgery, if any: none

Date of surgery: ~~sept. 23~~ Time ~~8 hrs~~ Degree of trauma: mild ☐ moderate X ☐ severe ☐

Anesthesia given: general

Exclusion criteria for participation in the study

Please check all items:

	YES	NO
__ Age below legal consent or over 70 years.	☐	X ☐
__ Confirmed pregnancy or a practical possibility of pregnancy	☐	X ☐
__ Hypersensitivity to salicylates or to the control medication	☐	X ☐
__ Current treatment with: systemic corticosteroid or anticoagulants.	☐	X ☐
__ Active peptic ulcer or g.i. hemorrhage.	☐	X ☐
__ Significant liver or kidney disease.	☐	X ☐
__ Hemopoietic disorders.	☐	X ☐

If none of these conditions applies to the patient, he or she may enter the study and receive test medication + instructions for use.

Start of treatment at onset of pain. DENTAL SURGERY FORM C

Diflunisal versus control Dr. M.L. McCUE

Investigator:

Name or initials: G.M. Study nr: 59

MEDICATION (please record times in 0-24 hours)

Test medication:

first dose was taken at	1200 hour on day of surgery				
second dose was taken at	~~1600~~ hour on day of surgery	X	*/ day after surgery	☐	
third dose was taken at	2000	-	☒	-	☐
fourth dose was taken at	0830	-	☐	-	X ☐
fifth dose was taken at	.....	-	☐	-	☐

If not all doses were used, give reason:

Did patient take any other analgesic since surgery? X No ; Yes

If yes, name of drug: Dose:

Time first dose was taken:

Did patient take strong alcoholic beverages X No Yes If yes, specify number of glasses:

Did patient use drugs for other diseases X No Yes If yes, specify: (name + dose)

FIGURE 61

DENTAL SURGERY FORM B

Start of treatment at onset of pain.

Diflunisal versus control

Name of investigator: Dr. M.L. McCUE

Name or initials: G.M. Study nr: 59

CONTROL VISIT Evaluation on of day after surgery date: sept. 24 hour: 1200
Only to be filled in if patient took test medication.

1. PATIENTS EVALUATION

Parameters	At intake of first dose of test medication	At control visit	Description of rating scales on opposite page.
1. Pain	1	1	
11. Patient's opinion on treatment efficacy		3	

11. ADVERSE REACTIONS

No~~xxx~~ or specify below:	Maximal intensity	Seriousness	Drug relationship	Action taken if any
Adverse reaction codes:	1 = mild 2 = moderate 3 = severe	1=not serious 2=serious	1=definitely not 2=probably not 3=possibly 4=probably 5=definitely	(e.g. dose reduction or discontinuation of test drug)

If adverse reaction was still present at control visit, give outcome if known (mandatory for serious reactions):

completely recovered
residual effects
reaction still present
died

patient receives treatment for reaction: yes; no
if yes, specify: _____

11. Investigator's overall evaluation taking into account expected spontaneous course of symptoms for individual patient.

Adverse reactions	Efficacy →	None	Poor	Fair	Good	Excellent
No adverse reactions	0				X	
Acceptable adverse reactions						
Unacceptable adverse reactions						

Comments, if any: patient was happy with the medication

FIGURE 62

Start of treatment at onset of pain. DENTAL SURGERY FORM A

Diflunisal versus control

To be completed on day of surgery

Name or Initials: G.T.	Age: 19 yrs.	Sex: X M F	Study nr: 60

Procedure: Removal of impacted tooth Impacted element: 18 28 38 48 75 85

Additional surgery, if any: none

Date of surgery: sept. 23 time am. Degree of trauma: mild ☐ moderate XX severe ☐

Anesthesia given: GENERAL

Exclusion criteria for participation in the study

Please check all items:

	YES	NO
__ Age below legal consent or over 70 years.	☐	XX
__ Confirmed pregnancy or a practical possibility of pregnancy	☐	XX
__ Hypersensitivity to salicylates or to the control medication	☐	XX
__ Current treatment with: systemic corticosteroid or anticoagulants.	☐	XX
__ Active peptic ulcer or g.i. hemorrhage.	☐	XX
__ Significant liver or kidney disease.	☐	XX
__ Hemopoietic disorders.	☐	XX

If none of these conditions applies to the patient, he or she may enter the study and receive test medication + instructions for use.

Start of treatment at onset of pain. DENTAL SURGERY FORM C

Diflunisal versus control

Investigator: Dr. M.L.MCCUE

Name or initials: G.T Study nr: 60

MEDICATION (please record times in 0-24 hours)

Test medication:

first dose was taken at 1400 hour on day of surgery

second dose was taken at .....hour on day of surgery ☐ */ day after surgery ☐

third dose was taken at ..... - ☐ - ☐

fourth dose was taken at ..... - ☐ - ☐

fifth dose was taken at ..... - ☐ - ☐

If not all doses were used, give reason: patient felt drug was not effective so changed to ,292,

Did patient take any other analgesic since surgery? No ; YXX

If yes, name of drug: 292 Dose: 1 tab

Time first dose was taken: 1430

Did patient take strong alcoholic beverages XX Yes If yes, specify number of glasses:

Did patient use drugs for other diseases XX Yes If yes, specify: (name + dose)

FIGURE 63

DENTAL SURGERY FORM B

Start of treatment at onset of pain.

Diflunisal versus control

Name of investigator: Dr. M.L. MCCUE

Name or initials: G.T. Study nr: 60

CONTROL VISIT Evaluation on of day after surgery date: Sept. 24 hour: 1200
only to be filled in if patient took test medication.

1. PATIENTS EVALUATION

Parameters	At intake of first dose of test medication	At control visit	Description of rating scales on opposite page.
1. Pain	4		
11. Patient's opinion on treatment efficacy		0	

11. ADVERSE REACTIONS

NONE, or specify below:	Maximal intensity	Seriousness	Drug relationship	Action taken if any
Adverse reaction codes:	1 = mild 2 = moderate 3 = severe	1=not serious 2=serious	1=definitely not 2=probably not 3=possibly 4=probably 5=definitely	(e.g. dose reduction or discontinuation of test drug)

If adverse reaction was still present at control visit, give outcome if known (mandatory for serious reactions):

completely recovered
residual effects
reaction still present
died

patient receives treatment for reaction: yes; no
if yes, specify:

11. Investigator's overall evaluation taking into account expected spontaneous course of symptoms for individual patient.

Adverse reactions Efficacy →	None	Poor	Fair	Good	Excellent
No adverse reactions	X				
Acceptable adverse reactions					
Unacceptable adverse reactions					

Comments, if any: patient changed to 292 one half hr. after taking 1st dose of medication . PATIENT did not give drug sufficient time to act

FIGURE 64

Start of treatment at onset of pain. DENTAL SURGERY FORM A

Diflunisal versus control

To be completed on day of surgery

Name or Initials: R.K.	Age: 22 yrs.	Sex: X M F	Study nr: 61

Procedure: Removal of impacted tooth Impacted element: 38 48

Additional surgery, if any: 18, 28

Date of surgery: Sept. 23 time A.M. Degree of trauma: mild XX moderate ☐ severe ☐

Anesthesia given: _____

Exclusion criteria for participation in the study

Please check all items:

	YES	NO
__ Age below legal consent or over 70 years.	☐	XX
__ Confirmed pregnancy or a practical possibility of pregnancy	☐	XXX
__ Hypersensitivity to salicylates or to the control medication	☐	XX
__ Current treatment with: systemic corticosteroid or anticoagulants.	☐	XX
__ Active peptic ulcer or g.i. hemorrhage.	☐	XX
__ Significant liver or kidney disease.	☐	XX
__ Hemopoietic disorders.	☐	XX

If none of these conditions applies to the patient, he or she may enter the study and receive test medication + instructions for use.

Start of treatment at onset of pain. DENTAL SURGERY FORM C

Diflunisal versus control

Investigator: Dr. M.L. MCCUE

Name or initials: R.K. Study nr: 61

MEDICATION (please record times in 0-24 hours)

Test medication:

first dose was taken at	1430 hour on day of surgery				
second dose was taken at	1830 hour on day of surgery	XX	*/ day after surgery	☐	
third dose was taken at	2230	=	XX	-	☐
fourth dose was taken at	0945	=	☐	-	XX
fifth dose was taken at	-----	=	☐	-	☐

If not all doses were used, give reason: _____

Did patient take any other analgesic since surgery? XX : Yes

If yes, name of drug: _____ Dose: _____

Time first dose was taken: _____

Did patient take strong alcoholic beverages XX Yes If yes, specify number of glasses: _____

Did patient use drugs for other diseases XX Yes If yes, specify: _____ (name + dose) _____

FIGURE 65

DENTAL SURGERY FORM B

Start of treatment at onset of pain.

Diflunisal versus control

Name of investigator: DR. M.L. MCCUE

Name or initials: R.K. Study nr: 61

CONTROL VISIT Evaluation on of day after surgery date: Sept. 24 hour: 1800
Only to be filled in if patient took test medication.

1. PATIENTS EVALUATION

Parameters	At intake of first dose of test medication	At control visit	Description of rating scales on opposite page.
1. Pain	3	2	
11. Patient's opinion on treatment efficacy	[illegible]	3	

11. ADVERSE REACTIONS

None, or specify below:	Maximal intensity	Seriousness	Drug relationship	Action taken if any
possible slight	1	1	2	none
headache				
Adverse reaction codes:	1 = mild 2 = moderate 3 = severe	1=not serious 2=serious	1=definitely not 2=probably not 3=possibly 4=probably 5=definitely	(e.g. dose reduction or discontinuation of test drug)

If adverse reaction was still present at control visit, give outcome if known (mandatory for serious reactions):

completely recovered
residual effects
reaction still present
died

patient receives treatment for reaction: yes; no
if yes, specify: _____

11. Investigator's overall evaluation taking into account expected spontaneous course of symptoms for individual patient.

Adverse reactions ↓ Efficacy →	None	Poor	Fair	Good	Excellent
No adverse reactions					
Acceptable adverse reactions				X	
Unacceptable adverse reactions					

Comments, if any: _____

FIGURE 66

Start of treatment at onset of pain. DENTAL SURGERY FORM A

Diflunisal versus control

To be completed on day of surgery

Name or Initials: D.P.	Age 21 yrs.	Sex: M X	Study nr: 62

Procedure: Removal of impacted tooth Impacted element: 28, 38, 48

Additional surgery, if any: 18

Date of surgery: Sept. 23 Time A.M. Degree of trauma: mild ☐ moderate ☐ severe ☒

Anesthesia given: GENERAL

Exclusion criteria for participation in the study

Please check all items:

	YES	NO
__ Age below legal consent or over 70 years.	☐	☒
__ Confirmed pregnancy or a practical possibility of pregnancy	☐	☒
__ Hypersensitivity to salicylates or to the control medication	☐	☒
__ Current treatment with: systemic corticosteroid or anticoagulants.	☐	☒
__ Active peptic ulcer or g.i. hemorrhage.	☐	☒
__ Significant liver or kidney disease.	☐	☒
__ Hemopoietic disorders.	☐	☒

If none of these conditions applies to the patient, he or she may enter the study and receive test medication + instructions for use.

Start of treatment at onset of pain. DENTAL SURGERY FORM C

Diflunisal versus control

Investigator: Dr. M.L. MCCUE

Name or initials: D.P. Study nr: 62

MEDICATION (please record times in 0-24 hours)

Test medication:

first dose was taken at 1500 hour on day of surgery

second dose was taken at 2145 hour on day of surgery ☒ */ day after surgery ☐

third dose was taken at 1150. " ☐ " ☒

fourth dose was taken at ..... " ☐ " ☐

fifth dose was taken at ..... " ☐ " ☐

If not all doses were used, give reason:

Did patient take any other analgesic since surgery? No ; XX

If yes, name of drug: 292 Dose: 1 tab

Time first dose was taken: 1300 sept. 24

Did patient take strong alcoholic beverages XX Yes If yes, specify number of glasses:

Did patient use drugs for other diseases XX Yes If yes, specify:

(name + dose)

FIGURE 67

DENTAL SURGERY FORM B

Start of treatment at onset of pain.

Diflunisal versus control

Name of investigator: Dr. M.L. MCCUE

Name or initials: D.P. Study nr: 62

CONTROL VISIT Evaluation on of day after surgery date: Sept. 24 hour: 1400
Only to be filled in if patient took test medication.

1. PATIENTS EVALUATION

Parameters	At intake of first dose of test medication	At control visit	Description of rating scales on opposite page.
1. Pain	2	4	
11. Patient's opinion on treatment efficacy		1	

11. ADVERSE REACTIONS

None, or specify below:	Maximal intensity	Seriousness	Drug relationship	Action taken if any
Adverse reaction codes:	1 = mild 2 = moderate 3 = severe	1=not serious 2=serious	1=definitely not 2=probably not 3=possibly 4=probably 5=definitely	(e.g. dose reduction or discontinuation of test drug)

If adverse reaction was still present at control visit, give outcome if known (mandatory for serious reactions):

completely recovered
residual effects
reaction still present
died

patient receives treatment for reaction: yes; no
if yes, specify: _____

11. Investigator's overall evaluation taking into account expected spontaneous course of symptoms for individual patient.

Adverse reactions	Efficacy →	None	Poor	Fair	Good	Excellent
No adverse reactions	0		X			
Acceptable adverse reactions						
Unacceptable adverse reactions						

Comments, if any: _____

FIGURE 68

Start of treatment at onset of pain. DENTAL SURGERY FORM A

Diflunisal versus control

To be completed on day of surgery

Name or Initials: M.F.	Age: 23 yrs.	Sex: M F	Study nr: 63

Procedure: Removal of impacted tooth Impacted element: 38, 48.

Additional surgery, if any: none

Date of surgery: sept. 23 Time: a.m. Degree of trauma: mild ☐ moderate ☒ severe ☐

Anesthesia given: general

Exclusion criteria for participation in the study

Please check all items:

	YES	NO
__ Age below legal consent or over 70 years.	☐	☒
__ Confirmed pregnancy or a practical possibility of pregnancy	☐	☒
__ Hypersensitivity to salicylates or to the control medication	☐	☒
__ Current treatment with: systemic corticosteroid or anticoagulants.	☐	☒
__ Active peptic ulcer or g.i. hemorrhage.	☐	☒
__ Significant liver or kidney disease.	☐	☒
__ Hemopoietic disorders.	☐	☒

If none of these conditions applies to the patient, he or she may enter the study and receive test medication + instructions for use.

Start of treatment at onset of pain. DENTAL SURGERY FORM C

Diflunisal versus control

Investigator: Dr. M.L. MCCUE

Name or Initials: M.F. Study nr: 63

MEDICATION (please record times in 0-24 hours)

Test medication:

first dose was taken at 1700. hour on day of surgery

second dose was taken at 2000 hour on day of surgery ☒ */ day after surgery ☐

third dose was taken at 2300. - ☒ - ☐

fourth dose was taken at 1000. - ☐ - ☒

fifth dose was taken at ..... - ☐ - ☐

If not all doses were used, give reason:

Did patient take any other analgesic since surgery ☒ No ; Yes

If yes, name of drug: Dose:

Time first dose was taken:

Did patient take strong alcoholic beverages ☒ No Yes If yes, specify number of glasses:

Did patient use drugs for other diseases ☒ No Yes If yes, specify:

(name + dose)

FIGURE 69

DENTAL SURGERY FORM B

Start of treatment at onset of pain.
Diflunisal versus control

Name of investigator: Dr. M.L. MCCUE

Name or initials: M.F. Study nr: 63

CONTROL VISIT Evaluation on of day after surgery date: Sept. 24 hour: 1300
Only to be filled in if patient took test medication.

1. PATIENTS EVALUATION

Parameters	At intake of first dose of test medication	At control visit	Description of rating scales on opposite page.
1. Pain	4	3	
11. Patient's opinion on treatment efficacy		1	

11. ADVERSE REACTIONS

None, or specify below:	Maximal intensity	Seriousness	Drug relationship	Action taken if any
Adverse reaction codes:	1 = mild 2 = moderate 3 = severe	1=not serious 2=serious	1=definitely not 2=probably not 3=possibly 4=probably 5=definitely	(e.g. dose reduction or discontinuation of test drug)

If adverse reaction was still present at control visit, give outcome if known (mandatory for serious reactions):

completely recovered
residual effects
reaction still present
died

patient receives treatment for reaction: yes; no
if yes, specify:

11. Investigator's overall evaluation taking into account expected spontaneous course of symptoms for individual patient.

Adverse reactions	Efficacy → None	Poor	Fair	Good	Excellent
No adverse reactions	0	X			
Acceptable adverse reactions					
Unacceptable adverse reactions					

Comments, if any: patient was not satisfied with the medication

FIGURE 70

Start of treatment at onset of pain. DENTAL SURGERY FORM A

Diflunisal versus control

To be completed on day of surgery

Name or Initials: E.P.	Age: 33 yrs.	Sex: M ☒	Study nr: 64

Procedure: Removal of impacted tooth Impacted element: 38, 48.

Additional surgery, if any: none

Date of surgery: sept. 23 time pm Degree of trauma: mild ☐ moderate ☐ severe ☒

Anesthesia given: general

Exclusion criteria for participation in the study

Please check all items:

	YES	NO
__ Age below legal consent or over 70 years.	☐	☒
__ Confirmed pregnancy or a practical possibility of pregnancy	☐	☒
__ Hypersensitivity to salicylates or to the control medication	☐	☒
__ Current treatment with: systemic corticosteroid or anticoagulants.	☐	☒
__ Active peptic ulcer or g.i. hemorrhage.	☐	☒
__ Significant liver or kidney disease.	☐	☒
__ Hemopoietic disorders.	☐	☒

If none of these conditions applies to the patient, he or she may enter the study and receive test medication + instructions for use.

Start of treatment at onset of pain. DENTAL SURGERY FORM C

Diflunisal versus control

Investigator: Dr. M.L. MCCUE

Name or initials: E.P. Study nr: 64

MEDICATION (please record times in 0-24 hours)

Test medication:

first dose was taken at 17.00 hour on day of surgery

second dose was taken at 2300 hour on day of surgery ☒ */ day after surgery ☐

third dose was taken at ..... = ☐ - ☐

fourth dose was taken at ..... = ☐ - ☐

fifth dose was taken at ..... = ☐ - ☐

If not all doses were used, give reason: no further doses required for pain

Did patient take any other analgesic since surgery? ~~No~~ ☒ ; Yes

If yes, name of drug: Dose:

Time first dose was taken:

Did patient take strong alcoholic beverages ~~No~~ ☒ Yes If yes, specify number of glasses:

Did patient use drugs for other diseases ~~No~~ ☒ Yes If yes, specify:

(name + dose)

FIGURE 71

DENTAL SURGERY FORM B

Start of treatment at onset of pain.

Diflunisal versus control

Name of investigator: Dr. M.L. MCCUE

Name or initials: E.P. Study nr: 64

CONTROL VISIT Evaluation on of day after surgery date: Sept. 24 hour: 1300
Only to be filled in if patient took test medication.

1. PATIENTS EVALUATION

Parameters	At intake of first dose of test medication	At control visit	Description of rating scales on opposite page.
1. Pain	2	1	
11. Patient's opinion on treatment efficacy		4	

11. ADVERSE REACTIONS

None or specify below:	Maximal intensity	Seriousness	Drug relationship	Action taken if any
Adverse reaction codes:	1 = mild 2 = moderate 3 = severe	1=not serious 2=serious	1=definitely not 2=probably not 3=possibly 4=probably 5=definitely	(e.g. dose reduction or discontinuation of test drug)

If adverse reaction was still present at control visit, give outcome if known (mandatory for serious reactions):

completely recovered
residual effects
reaction still present
died

patient receives treatment for reaction: yes; no
if yes, specify:

11. Investigator's overall evaluation taking into account expected spontaneous course of symptoms for individual patient.

Adverse reactions ↓ Efficacy →	None	Poor	Fair	Good	Excellent
No adverse reactions	0				X
Acceptable adverse reactions					
Unacceptable adverse reactions					

Comments, if any: patient was extremely happy with the medication

FIGURE 72

Start of treatment at onset of pain. DENTAL SURGERY FORM A

Diflunisal versus control

To be completed on day of surgery

Name or Initials: B.H.	Age: 19 yrs.	Sex: M X	Study nr: 65

Procedure: Removal of impacted tooth Impacted element: 18, 28, 38, 48

Additional surgery, if any: none

Date of surgery: sept. 23 time a.m. Degree of trauma: mild ☐ moderate ☒ severe ☐

Anesthesia given:

Exclusion criteria for participation in the study

Please check all items:

	YES	NO
__ Age below legal consent or over 70 years.	☐	☒
__ Confirmed pregnancy or a practical possibility of pregnancy	☐	☒
__ Hypersensitivity to salicylates or to the control medication	☐	☒
__ Current treatment with: systemic corticosteroid or anticoagulants.	☐	☒
__ Active peptic ulcer or g.i. hemorrhage.	☐	☒
__ Significant liver or kidney disease.	☐	☒
__ Hemopoietic disorders.	☐	☒

If none of these conditions applies to the patient, he or she may enter the study and receive test medication + instructions for use.

Start of treatment at onset of pain. DENTAL SURGERY FORM C

Diflunisal versus control

Investigator:

Name or initials: B.H. Study nr: 65

MEDICATION (please record times in 0-24 hours)

Test medication:

first dose was taken at 1730 hour on day of surgery

second dose was taken at 2140 hour on day of surgery ☒ */ day after surgery ☐

third dose was taken at 0300	-	☐	-	☒
fourth dose was taken at 0930	-	☐	-	☒
fifth dose was taken at	-	☐	-	☐

If not all doses were used, give reason:

Did patient take any other analgesic since surgery? ~~XX~~ No ; Yes

If yes, name of drug: Dose:

Time first dose was taken:

Did patient take strong alcoholic beverages ~~XX~~ Yes If yes, specify number of glasses:

Did patient use drugs for other diseases ~~XX~~ Yes If yes, specify:

(name + dose)

FIGURE 73

DENTAL SURGERY FORM B

Start of treatment at onset of pain.

Diflunisal versus control

Name of investigator: Dr. M.L. MCCUE

Name or initials: B.H. Study nr: 65

CONTROL VISIT Evaluation on of day after surgery date: sept. 24 hour: 1800
Only to be filled in if patient took test medication.

1. PATIENTS EVALUATION

Parameters	At intake of first dose of test medication	At control visit	Description of rating scales on opposite page.
1. Pain	2	3	
11. Patient's opinion on treatment efficacy		2	

11. ADVERSE REACTIONS

None, or specify below:	Maximal intensity	Seriousness	Drug relationship	Action taken if any
Adverse reaction codes:	1 = mild 2 = moderate 3 = severe	1=not serious 2=serious	1=definitely not 2=probably not 3=possibly 4=probably 5=definitely	(e.g. dose reduction or discontinuation of test drug)

If adverse reaction was still present at control visit, give outcome if known (mandatory for serious reactions):

completely recovered
residual effects
reaction still present
died

patient receives treatment for reaction: yes; no
if yes, specify:

11. Investigator's overall evaluation taking into account expected spontaneous course of symptoms for individual patient.

Adverse reactions	Efficacy →	None	Poor	Fair	Good	Excellent
No adverse reactions	0			X		
Acceptable adverse reactions						
Unacceptable adverse reactions						

Comments, if any:

FIGURE 74

Start of treatment at onset of pain. DENTAL SURGERY FORM A

Diflunisal versus control

To be completed on day of surgery

Name or Initials: S.M.	Age: 19 yrs.	Sex: M F X	Study nr: 66

Procedure: Removal of impacted tooth Impacted element: 18, 28, 38, 48

Additional surgery, if any: none

Date of surgery: sept 23 time ___ am Degree of trauma: mild ☐
moderate ☒
severe ☐

Anesthesia given: general

Exclusion criteria for participation in the study

Please check all items:

	YES	NO
__ Age below legal consent or over 70 years.	☐	☒
__ Confirmed pregnancy or a practical possibility of pregnancy	☐	☒
__ Hypersensitivity to salicylates or to the control medication	☐	☒
__ Current treatment with: systemic corticosteroid or anticoagulants.	☐	☒
__ Active peptic ulcer or g.i. hemorrhage.	☐	☒
__ Significant liver or kidney disease.	☐	☒
__ Hemopoietic disorders.	☐	☒

If none of these conditions applies to the patient, he or she may enter the study and receive test medication + instructions for use.

Start of treatment at onset of pain. DENTAL SURGERY FORM C

Diflunisal versus control

Investigator: Dr. M.L. MCCOE

Name or initials: S.M. Study nr: 66

MEDICATION (please record times in 0-24 hours)

Test medication:

first dose was taken at 1530 hour on day of surgery

second dose was taken at 2230 hour on day of surgery ☒ */ day after surgery ☐

third dose was taken at	1000	-	☐	-	☒
fourth dose was taken at	.....	-	☐	-	☐
fifth dose was taken at	.....	-	☐	-	☐

If not all doses were used, give reason: _____

Did patient take any other analgesic since surgery? ~~XX~~ ; Yes

If yes, name of drug: _____ Dose: _____

Time first dose was taken: _____

Did patient take strong alcoholic beverages ~~XX~~ Yes If yes, specify number of glasses: _____

Did patient use drugs for other diseases ~~XX~~ Yes If yes, specify: _____

(name + dose) _____

FIGURE 75

DENTAL SURGERY FORM B

Start of treatment at onset of pain.

Diflunisal versus control

Name of investigator: Dr. M.L. MCCUE

Name or initials: S.M. Study nr: 66

CONTROL VISIT Evaluation on of day after surgery date: sept.24 hour: 1200
Only to be filled in if patient took test medication.

1. PATIENTS EVALUATION

Parameters	At intake of first dose of test medication	At control visit	Description of rating scales on opposite page.
1. Pain	4	1	
11. Patient's opinion on treatment efficacy		4	

11. ADVERSE REACTIONS

~~None~~ or specify below:	Maximal intensity	Seriousness	Drug relationship	Action taken if any
Adverse reaction codes:	1 = mild 2 = moderate 3 = severe	1=not serious 2=serious	1=definitely not 2=probably not 3=possibly 4=probably 5=definitely	(e.g. dose reduction or discontinuation of test drug)

If adverse reaction was still present at control visit, give outcome if known (mandatory for serious reactions):

completely recovered
residual effects
reaction still present
died

patient receives treatment for reaction: yes; no
if yes, specify:

11. Investigator's overall evaluation taking into account expected spontaneous course of symptoms for individual patient.

Adverse reactions Efficacy →	None	Poor	Fair	Good	Excellent
No adverse reactions					
Acceptable adverse reactions					
Unacceptable adverse reactions					

Comments, if any: patient was very happy with the medication

FIGURE 76

Start of treatment at onset of pain. DENTAL SURGERY FORM A

Diflunisal versus control

To be completed on day of surgery

Name or Initials: D.H.	Age: 18 yrs.	Sex: M F	Study nr: 67

Procedure: Removal of impacted tooth Impacted element: 18, 28, 38, 48.

Additional surgery, if any: none

Date of surgery: sept. 28 time am Degree of trauma: mild ☐ moderate ☒ severe ☐

Anesthesia given: general

Exclusion criteria for participation in the study

Please check all items:

	YES	NO
__ Age below legal consent or over 70 years.	☐	☒
__ Confirmed pregnancy or a practical possibility of pregnancy	☐	☒
__ Hypersensitivity to salicylates or to the control medication	☐	☒
__ Current treatment with: systemic corticosteroid or anticoagulants.	☐	☒
__ Active peptic ulcer or g.i. hemorrhage.	☐	☒
__ Significant liver or kidney disease.	☐	☒
__ Hemopoietic disorders.	☐	☒

If none of these conditions applies to the patient, he or she may enter the study and receive test medication + instructions for use.

Start of treatment at onset of pain. DENTAL SURGERY FORM C

Diflunisal versus control

Investigator: Dr. M.L. MCCUE

Name or initials: D.H. Study nr: 67

MEDICATION (please record times in 0-24 hours)

Test medication:

first dose was taken at 1725..hour on day of surgery

second dose was taken at 2400.....hour on day of surgery ☐*/ day after surgery ☐

third dose was taken at 0330.. - ☐ - ☒

fourth dose was taken at ..... - ☐ - ☐

fifth dose was taken at ..... - ☐ - ☐

If not all doses were used, give reason:

Did patient take any other analgesic since surgery? No : Yes XXX

If yes, name of drug: 222 Dose: 2 tabs

Time first dose was taken: sept. 29 pm.

Did patient take strong alcoholic beverages ~~No~~ Yes If yes, specify number of glasses:

Did patient use drugs for other diseases No Yes XXX If yes, specify: tetracyclene

(name + dose)

FIGURE 77

DENTAL SURGERY FORM B

Start of treatment at onset of pain.

Diflunisal versus control

Name of investigator: Dr. M.L. MCCUE

Name or initials: D.H. Study nr: 67

CONTROL VISIT Evaluation on of day after surgery date: sept.29 hour: 1900
Only to be filled in if patient took test medication.

1. PATIENTS EVALUATION

Parameters	At intake of first dose of test medication	At control visit	Description of rating scales on opposite page.
1. Pain	2	1	
11. Patient's opinion on treatment efficacy		3	

11. ADVERSE REACTIONS

~~None~~ or specify below:	Maximal intensity	Seriousness	Drug relationship	Action taken if any
Adverse reaction codes:	1 = mild 2 = moderate 3 = severe	1=not serious 2=serious	1=definitely not 2=probably not 3=possibly 4=probably 5=definitely	(e.g. dose reduction or discontinuation of test drug)

If adverse reaction was still present at control visit, give outcome if known (mandatory for serious reactions):

completely recovered
residual effects
reaction still present
died

patient receives treatment for reaction: yes; no
if yes, specify: _____

11. Investigator's overall evaluation taking into account expected spontaneous course of symptoms for individual patient.

Adverse reactions	Efficacy →	None	Poor	Fair	Good	Excellent
No adverse reactions	0				X	
Acceptable adverse reactions						
Unacceptable adverse reactions						

Comments, if any: _____

FIGURE 78

Start-of treatment at onset of pain. DENTAL SURGERY FORM A

Diflunisal versus control

To be completed on day of surgery

Name or Initials: B.N.	Age: 23 yrs.	Sex: M X	Study nr: 68

Procedure: Removal of impacted tooth Impacted element: 38, 48.

Additional surgery, if any: none

Date of surgery: sept 28 time ___ am. Degree of trauma: wild XX
moderate ☐
severe ☐

Anesthesia given: general

Exclusion criteria for participation in the study

Please check all items:

	YES	NO
___ Age below legal consent or over 70 years.	☐	☒
___ Confirmed pregnancy or a practical possibility of pregnancy	☐	☒
___ Hypersensitivity to salicylates or to the control medication	☐	☒
___ Current treatment with: systemic corticosteroid or anticoagulants.	☐	☒
___ Active peptic ulcer or g.i. hemorrhage.	☐	☒
___ Significant liver or kidney disease.	☐	☒
___ Hemopoietic disorders.	☐	☒

If none of these conditions applies to the patient, he or she may enter the study and receive test medication + instructions for use.

Start of treatment at onset of pain. DENTAL SURGERY FORM C

Diflunisal versus control

Investigator: Dr. M.L. MCCUE

Name or initials: B.N. Study nr: 68

MEDICATION (please record times in 0-24 hours)

Test medication:

first dose was taken at 1520 ...hour on day of surgery

second dose was taken at 2100 ..hour on day of surgery ☒ */ day after surgery ☐

third dose was taken at 0130 .. - ☐ - ☒

fourth dose was taken at 0915 ..... - ☐ - ☒

fifth dose was taken at ..... - ☐ - ☐

If not all doses were used, give reason: ___

Did patient take any other analgesic since surgery? XXX ; Yes

If yes, name of drug: ___ Dose: ___

Time first dose was taken: ___

Did patient take strong alcoholic beverages? XX No Yes If yes, specify number of glasses: ___

Did patient use drugs for other diseases No XXX If yes, specify: furodantin
(name + dose) 50 mg.

FIGURE 79

DENTAL SURGERY FORM B

Start of treatment at onset of pain.
Diflunisal versus control

Name of investigator: Dr. M.L. MCCUE

Name or initials: B.N. Study nr: 68

CONTROL VISIT Evaluation on of day after surgery date: sept. 29 hour: 1200
Only to be filled in if patient took test medication.

1. PATIENTS EVALUATION

Parameters	At intake of first dose of test medication	At control visit	Description of rating scales on opposite page.
1. Pain	3	3	
11. Patient's opinion on treatment efficacy	[illegible]	2	

11. ADVERSE REACTIONS

None or specify below:	Maximal intensity	Seriousness	Drug relationship	Action taken if any
Adverse reaction codes:	1 = mild 2 = moderate 3 = severe	1=not serious 2=serious	1=definitely not 2=probably not 3=possibly 4=probably 5=definitely	(e.g. dose reduction or discontinuation of test drug)

If adverse reaction was still present at control visit, give outcome if known (mandatory for serious reactions):

completely recovered
residual effects
reaction still present
died

patient receives treatment for reaction: yes; no
if yes, specify:

11. Investigator's overall evaluation taking into account expected spontaneous course of symptoms for individual patient.

Adverse reactions	Efficacy → None	Poor	Fair	Good	Excellent
No adverse reactions	0				
Acceptable adverse reactions					
Unacceptable adverse reactions					

Comments, if any: patient received only slight relief from the medication

FIGURE 80

Start of treatment at onset of pain. DENTAL SURGERY FORM A

Diflunisal versus control

To be completed on day of surgery

Name or Initials: M.S.	Age: 25 yrs.	Sex: F M	Study nr: 69

Procedure: Removal of impacted tooth Impacted element: 48

Additional surgery, if any: 18, 28, 38.

Date of surgery: sept. 28 time ~~a.m.~~ Degree of trauma: mild ☒

moderate ☐

Anesthesia given: general severe ☐

Exclusion criteria for participation in the study

Please check all items:

	YES	NO
__ Age below legal consent or over 70 years.	☐	☒
__ Confirmed pregnancy or a practical possibility of pregnancy	☐	☒
__ Hypersensitivity to salicylates or to the control medication	☐	☒
__ Current treatment with: systemic corticosteroid or anticoagulants.	☐	☒
__ Active peptic ulcer or g.i. hemorrhage.	☐	☒
__ Significant liver or kidney disease.	☐	☒
__ Hemopoietic disorders.	☐	☒

If none of these conditions applies to the patient, he or she may enter the study and receive test medication + instructions for use.

Start of treatment at onset of pain. DENTAL SURGERY FORM C

Dr. M.L. McGUIGAN Diflunisal versus control

Investigator:

Name or initials: M.S. Study nr: 69

MEDICATION (please record times in 0-24 hours)

Test medication:

first dose was taken at 1700 ....hour on day of surgery

second dose was taken at 2300 hour on day of surgery ☐ */ day after surgery ☐

third dose was taken at ..... = ☐ - ☐

fourth dose was taken at ..... = ☐ - ☐

fifth dose was taken at ..... = ☐ - ☐

If not all doses were used, give reason: no further doses required for pain

Did patient take any other analgesic since surgery? ☒ No : Yes

If yes, name of drug: Dose:

Time first dose was taken:

Did patient take strong alcoholic beverages? ☒ No Yes If yes, specify number of glasses:

Did patient use drugs for other diseases ☒ No Yes If yes, specify:

(name + dose)

FIGURE 81

DENTAL SURGERY FORM B

Start of treatment at onset of pain.

Diflunisal versus control

Name of investigator: Dr. M.L. McCUE

Name or initials: M.S. Study nr: 69

CONTROL VISIT Evaluation on of day after surgery date: sept. 29 hour: 1200
Only to be filled in if patient took test medication.

I. PATIENTS EVALUATION

Parameters	At intake of first dose of test medication	At control visit	Description of rating scales on opposite page.
1. Pain	3	0	
11. Patient's opinion on treatment efficacy	[illegible]	3	

11. ADVERSE REACTIONS

None or specify below:	Maximal intensity	Seriousness	Drug relationship	Action taken if any
Adverse reaction codes:	1 = mild 2 = moderate 3 = severe	1=not serious 2=serious	1=definitely not 2=probably not 3=possibly 4=probably 5=definitely	(e.g. dose reduction or discontinuation of test drug)

If adverse reaction was still present at control visit, give outcome if known (mandatory for serious reactions):

completely recovered
residual effects
reaction still present
died

patient receives treatment for reaction: yes; no
if yes, specify:

11. Investigator's overall evaluation taking into account expected spontaneous course of symptoms for individual patient.

Adverse reactions	Efficacy → None	Poor	Fair	Good	Excellent
No adverse reactions	0				X
Acceptable adverse reactions					
Unacceptable adverse reactions					

Comments, if any: patient was happy with the medication

FIGURE 82

Start of treatment at onset of pain. DENTAL SURGERY FORM A

Diflunisal versus control

To be completed on day of surgery

Name or Initials: D.E.	Age 18 yrs.	Sex: F M	Study nr: 70

Procedure: Removal of impacted tooth Impacted element: 18, 28, 38, 48.

Additional surgery, if any: none

Date of surgery: sept. 28 ~~19~~ a.m. Degree of trauma: mild X
moderate
severe

Anesthesia given: general

Exclusion criteria for participation in the study

Please check all items:

	YES	NO
__ Age below legal consent or over 70 years.	☐	X
__ Confirmed pregnancy or a practical possibility of pregnancy	☐	X
__ Hypersensitivity to salicylates or to the control medication	☐	X
__ Current treatment with: systemic corticosteroid or anticoagulants.	☐	X
__ Active peptic ulcer or g.i. hemorrhage.	☐	X
__ Significant liver or kidney disease.	☐	X
__ Hemopoietic disorders.	☐	X

If none of these conditions applies to the patient, he or she may enter the study and receive test medication + instructions for use.

Start of treatment at onset of pain. DENTAL SURGERY FORM C

Diflunisal versus control

Investigator: Dr. M.L. MCGUE

Name or initials: D.E. Study nr: 70

MEDICATION (please record times in 0-24 hours)

Test medication:

first dose was taken at	1800	hour on day of surgery			
second dose was taken at	2200	hour on day of surgery X	*/ day after surgery		
third dose was taken at	0200	-	☐	-	X
fourth dose was taken at	0815	-	☐	-	X
fifth dose was taken at	.....	-	☐	-	☐

If not all doses were used, give reason:

Did patient take any other analgesic since surgery? No ; X Yes

If yes, name of drug: 292 Dose: 1 tab

Time first dose was taken: 1300 sept. 29

Did patient take strong alcoholic beverages No X Yes If yes, specify number of glasses:

Did patient use drugs for other diseases No X Yes If yes, specify: flagyl

(name + dose) 50 mg.

FIGURE 83

DENTAL SURGERY FORM B

Start of treatment at onset of pain.

Diflunisal versus control

Name of investigator: Dr. M.L. McCUE

Name or initials: D.E. Study nr: 70

CONTROL VISIT Evaluation on of day after surgery date: sept. 29 hour: 1900
Only to be filled in if patient took test medication.

1. PATIENTS EVALUATION

Parameters	At intake of first dose of test medication	At control visit	Description of rating scales on opposite page.
1. Pain	4	1	
11. Patient's opinion on treatment efficacy		4	

11. ADVERSE REACTIONS

None, or specify below:	Maximal intensity	Seriousness	Drug relationship	Action taken if any
Adverse reaction codes:	1 = mild 2 = moderate 3 = severe	1=not serious 2=serious	1=definitely not 2=probably not 3=possibly 4=probably 5=definitely	(e.g. dose reduction or discontinuation of test drug)

If adverse reaction was still present at control visit, give outcome if known (mandatory for serious reactions):

completely recovered
residual effects
reaction still present
died

patient receives treatment for reaction: yes; no
if yes, specify:

11. Investigator's overall evaluation taking into account expected spontaneous course of symptoms for individual patient.

Adverse reactions	Efficacy →	None	Poor	Fair	Good	Excellent
No adverse reactions	0		X			
Acceptable adverse reactions						
Unacceptable adverse reactions						

Comments, if any: patient was not satisfied with the medication

FIGURE 84

Start of treatment at onset of pain. DENTAL SURGERY FORM A

Diflunisal versus control

To be completed on day of surgery

Name or Initials: C. H.	Age: 19 yrs.	Sex: F M	Study nr: 71

Procedure: Removal of impacted tooth Impacted element: 18, 28, 38, 48.

Additional surgery, if any: none

Date of surgery: sept 30 time p.m. Degree of trauma: mild X
moderate ☐
severe ☐

Anesthesia given: general

Exclusion criteria for participation in the study

Please check all items:

	YES	NO
__ Age below legal consent or over 70 years.	☐	X
__ Confirmed pregnancy or a practical possibility of pregnancy	☐	X
__ Hypersensitivity to salicylates or to the control medication	☐	X
__ Current treatment with: systemic corticosteroid or anticoagulants.	☐	X
__ Active peptic ulcer or g.i. hemorrhage.	☐	X
__ Significant liver or kidney disease.	☐	X
__ Hemopoietic disorders.	☐	X

If none of these conditions applies to the patient, he or she may enter the study and receive test medication + instructions for use.

Start of treatment at onset of pain. DENTAL SURGERY FORM C

Diflunisal versus control

Investigator: Dr. M.L. McCUE

Name or Initials: C.H. Study nr: 71

MEDICATION (please record times in 0-24 hours)

Test medication:

first dose was taken at	1530 hour on day of surgery				
second dose was taken at	1900 hour on day of surgery	X	*/ day after surgery	☐	
third dose was taken at	0100	-	☐	-	X
fourth dose was taken at	1030	-	☐	-	X
fifth dose was taken at	.....	-	☐	-	☐

If not all doses were used, give reason:

Did patient take any other analgesic since surgery? No X : Yes

If yes, name of drug: Dose:

Time first dose was taken:

Did patient take strong alcoholic beverages? No X Yes If yes, specify number of glasses:

Did patient use drugs for other diseases X No Yes If yes, specify:
(name + dose)

FIGURE 85

DENTAL SURGERY FORM B

Start of treatment at onset of pain.

Diflunisal versus control

Name of investigator: D.. M.L. McCUE

Name or initials: C.H. Study nr: 71

CONTROL VISIT Evaluation on of day after surgery date: oct.1 hour: 1100
Only to be filled in if patient took test medication.

1. PATIENTS EVALUATION

Parameters	At intake of first dose of test medication	At control visit	Description of rating scales on opposite page.
1. Pain	2	2	
11. Patient's opinion on treatment efficacy		1	

11. ADVERSE REACTIONS

None, or specify below: XX	Maximal intensity	Seriousness	Drug relationship	Action taken if any
Adverse reaction codes:	1 = mild 2 = moderate 3 = severe	1=not serious 2=serious	1=definitely not 2=probably not 3=possibly 4=probably 5=definitely	(e.g. dose reduction or discontinuation of test drug)

If adverse reaction was still present at control visit, give outcome if known (mandatory for serious reactions):

completely recovered
residual effects
reaction still present
died

patient receives treatment for reaction: yes; no
if yes, specify:

11. Investigator's overall evaluation taking into account expected spontaneous course of symptoms for individual patient.

Adverse reactions Efficacy →	None	Poor	Fair	Good	Excellent
No adverse reactions		X			
Acceptable adverse reactions					
Unacceptable adverse reactions					

Comments, if any: patient was not too happy with the results even though the pain was not severe

FIGURE 86

Start of treatment at onset of pain. DENTAL SURGERY FORM A

Diflunisal versus control

To be completed on day of surgery

Name or Initials: F.M.	Age: 21 yrs.	Sex: M F	Study nr: 72

Procedure: Removal of impacted tooth Impacted element: 38, 48.

Additional surgery, if any: none

Date of surgery: sept. 30 time a.m. Degree of trauma: mild ☒ moderate ☐ severe ☐

Anesthesia given: general

Exclusion criteria for participation in the study

Please check all items:

	YES	NO
__ Age below legal consent or over 70 years.	☐	☒
__ Confirmed pregnancy or a practical possibility of pregnancy	☐	☒
__ Hypersensitivity to salicylates or to the control medication	☐	☒
__ Current treatment with: systemic corticosteroid or anticoagulants.	☐	☒
__ Active peptic ulcer or g.i. hemorrhage.	☐	☒
__ Significant liver or kidney disease.	☐	☒
__ Hemopoietic disorders.	☐	☒

If none of these conditions applies to the patient, he or she may enter the study and receive test medication + instructions for use.

Start of treatment at onset of pain. DENTAL SURGERY FORM C

Diflunisal versus control

Investigator: Dr. M.L. McCUE

Name or initials: F.M. Study nr: 72

MEDICATION (please record times in 0-24 hours)

Test medication:

first dose was taken at 1515 hour on day of surgery

second dose was taken at 2115 hour on day of surgery ☒ */ day after surgery ☐

third dose was taken at ..... - ☐ - ☒

fourth dose was taken at ..... - ☐ - ☐

fifth dose was taken at ..... - ☐ - ☐

If not all doses were used, give reason:

Did patient take any other analgesic since surgery? ☒ No ; ☐ Yes

If yes, name of drug: Dose:

Time first dose was taken:

Did patient take strong alcoholic beverages ☒ No ☐ Yes If yes, specify number of glasses:

Did patient use drugs for other diseases ☒ No ☐ Yes If yes, specify:

(name + dose)

FIGURE 87

DENTAL SURGERY FORM B

Start of treatment at onset of pain.

Diflunisal versus control

Name of investigator: Dr. M.L. McCUE

Name or initials: F.M. Study nr: 72

CONTROL VISIT Evaluation on of day after surgery date: oct. 1 hour: 1600
Only to be filled in if patient took test medication.

1. PATIENTS EVALUATION

Parameters	At intake of first dose of test medication	At control visit	Description of rating scales on opposite page.
1. Pain	4	1	
11. Patient's opinion on treatment efficacy		3	

11. ADVERSE REACTIONS

None, or specify below: XX	Maximal intensity	Seriousness	Drug relationship	Action taken if any
Adverse reaction codes:	1 = mild 2 = moderate 3 = severe	1=not serious 2=serious	1=definitely not 2=probably not 3=possibly 4=probably 5=definitely	(e.g. dose reduction or discontinuation of test drug)

If adverse reaction was still present at control visit, give outcome if known (mandatory for serious reactions):

completely recovered
residual effects
reaction still present
died

patient receives treatment for reaction: yes; no
if yes, specify:

11. Investigator's overall evaluation taking into account expected spontaneous course of symptoms for individual patient.

Adverse reactions Efficacy →	None	Poor	Fair	Good	Excellent
No adverse reactions				X	
Acceptable adverse reactions					
Unacceptable adverse reactions					

Comments, if any:

FIGURE 88

Start of treatment at onset of pain. DENTAL SURGERY FORM A

Diflunisal versus control

To be completed on day of surgery

Name or Initials: J.S.	Age 18 yrs.	Sex: F M	Study nr: 73

Procedure: Removal of impacted tooth Impacted element: 18, 28, 38, 48.

Additional surgery, if any: none

Date of surgery: ~~sept. 30~~ time ~~a.m.~~ Degree of trauma: mild ☐ moderate ☐ severe ☒

Anesthesia given: general

Exclusion criteria for participation in the study

Please check all items:

	YES	NO
__ Age below legal consent or over 70 years.	☐	☒
__ Confirmed pregnancy or a practical possibility of pregnancy	☐	☒
__ Hypersensitivity to salicylates or to the control medication	☐	☒
__ Current treatment with: systemic corticosteroid or anticoagulants.	☐	☒
__ Active peptic ulcer or g.i. hemorrhage.	☐	☒
__ Significant liver or kidney disease.	☐	☒
__ Hemopoietic disorders.	☐	☒

If none of these conditions applies to the patient, he or she may enter the study and receive test medication + instructions for use.

Start of treatment at onset of pain. DENTAL SURGERY FORM C

Diflunisal versus control

Investigator: Dr. M.L. MCCUE

Name or initials: J.S. Study nr: 73

MEDICATION (please record times in 0-24 hours)

Test medication:

first dose was taken at 1600 hour on day of surgery

second dose was taken at 2030 hour on day of surgery ☒ */ day after surgery ☐

third dose was taken at ..... - ☐ - ☒

fourth dose was taken at 0830 - ☐ - ☒

fifth dose was taken at ..... - ☐ - ☐

If not all doses were used, give reason:

Did patient take any other analgesic since surgery? ☒ No ; Yes

If yes, name of drug: Dose:

Time first dose was taken:

Did patient take strong alcoholic beverages? ☒ No Yes If yes, specify number of glasses:

Did patient use drugs for other diseases ☒ No Yes If yes, specify:

(name + dose)

FIGURE 89

DENTAL SURGERY FORM B

Start of treatment at onset of pain.

Diflunisal versus control

*Name of investigator: Dr. M.L. McCUE

Name or initials: J.S. Study nr: 73

CONTROL VISIT · Evaluation on of day after surgery date: OCT.1 hour: 1100
Only to be filled in if patient took test medication.

1. PATIENTS EVALUATION

Parameters	At intake of first dose of test medication	At control visit	Description of rating scales on opposite page.
1. Pain	2	3	
11. Patient's opinion on treatment efficacy		1	

11. ADVERSE REACTIONS

None, or specify below:	Maximal intensity	Seriousness	Drug relationship	Action taken if any
Adverse reaction codes:	1 = mild 2 = moderate 3 = severe	1=not serious 2=serious	1=definitely not 2=probably not 3=possibly 4=probably 5=definitely	(e.g. dose reduction or discontinuation of test drug)

If adverse reaction was still present at control visit, give outcome if known (mandatory for serious reactions):

completely recovered
residual effects
reaction still present
died

patient receives treatment for reaction: yes; no
if yes, specify:

11. Investigator's overall evaluation taking into account expected spontaneous course of symptoms for individual patient.

Adverse reactions	Efficacy →	None	Poor	Fair	Good	Excellent
No adverse reactions	0	X				
Acceptable adverse reactions						
Unacceptable adverse reactions						

Comments, if any: ~~patient was not satisfied with the medication~~

FIGURE 90

Start of treatment at onset of pain. DENTAL SURGERY FORM A

Diflunisal versus control

To be completed on day of surgery

Name or Initials: L.S.	Age: 24 yrs.	Sex: F M	Study nr: 74

Procedure: Removal of impacted tooth Impacted element: 28, 38.

Additional surgery, if any: none

Date of surgery: sept. 30 time AM. Degree of trauma: mild ☐ moderate ☒ severe ☐

Anesthesia given: general

Exclusion criteria for participation in the study

Please check all items:

	YES	NO
__ Age below legal consent or over 70 years.	☐	☒
__ Confirmed pregnancy or a practical possibility of pregnancy	☐	☒
__ Hypersensitivity to salicylates or to the control medication	☐	☒
__ Current treatment with: systemic corticosteroid or anticoagulants.	☐	☒
__ Active peptic ulcer or g.i. hemorrhage.	☐	☒
__ Significant liver or kidney disease.	☐	☒
__ Hemopoietic disorders.	☐	☒

If none of these conditions applies to the patient, he or she may enter the study and receive test medication + instructions for use.

Start of treatment at onset of pain. DENTAL SURGERY FORM C

Diflunisal versus control

Investigator: Dr. M.L. McCUE

Name or initials: L.S. Study nr: 74

MEDICATION (please record times in 0-24 hours)

Test medication:

first dose was taken at 1800 hour on day of surgery

second dose was taken at 2400 hour on day of surgery ☒ 1 day after surgery ☐

third dose was taken at ..... = ☐ = ☐

fourth dose was taken at ..... = ☐ = ☐

fifth dose was taken at ..... = ☐ = ☐

If not all doses were used, give reason: did not require further doses for pain

Did patient take any other analgesic since surgery? ☒ No ; Yes

If yes, name of drug: Dose:

Time first dose was taken:

Did patient take strong alcoholic beverages? ☒ No Yes If yes, specify number of glasses:

Did patient use drugs for other diseases ☒ No Yes If yes, specify: (name + dose)

FIGURE 91

DENTAL SURGERY FORM B

Start of treatment at onset of pain.

Diflunisal versus control

Name of investigator: Dr. M.L. McCUE

Name or initials: L.S. Study nr: 74

CONTROL VISIT Evaluation on of day after surgery date: oct. 1 hour: 1100
Only to be filled in if patient took test medication.

1. PATIENTS EVALUATION

Parameters	At intake of first dose of test medication	At control visit	Description of rating scales on opposite page.
1. Pain	2	0	
11. Patient's opinion on treatment efficacy		3	

11. ADVERSE REACTIONS

XXXX None, or specify below:	Maximal intensity	Seriousness	Drug relationship	Action taken if any
Adverse reaction codes:	1 = mild 2 = moderate 3 = severe	1=not serious 2=serious	1=definitely not 2=probably not 3=possibly 4=probably 5=definitely	(e.g. dose reduction or discontinuation of test drug)

If adverse reaction was still present at control visit, give outcome if known (mandatory for serious reactions):

completely recovered
residual effects
reaction still present
died

patient receives treatment for reaction: yes; no
if yes, specify:

11. Investigator's overall evaluation taking into account expected spontaneous course of symptoms for individual patient.

Adverse reactions	Efficacy →	None	Poor	Fair	Good	Excellent
No adverse reactions	0				X	
Acceptable adverse reactions						
Unacceptable adverse reactions						

Comments, if any: patient felt that the onset was slow but the effectiveness was good once analgesia was obtained

FIGURE 92

Start of treatment at onset of pain. DENTAL SURGERY FORM A

Diflunisal versus control

To be completed on day of surgery

Name or Initials: J.L.	Age: 23 yrs.	Sex: F M	Study nr: 75

Procedure: Removal of impacted tooth Impacted element: 38

Additional surgery, if any: none

Date of surgery: oct.4 time am. Degree of trauma: mild ☐ moderate XX ☐ severe ☐

Anesthesia given: local anaesth. and I.V. sedation

Exclusion criteria for participation in the study

Please check all items:

	YES	NO
__ Age below legal consent or over 70 years.	☐	X ☐
__ Confirmed pregnancy or a practical possibility of pregnancy	☐	X ☐
__ Hypersensitivity to salicylates or to the control medication	☐	X ☐
__ Current treatment with: systemic corticosteroid or anticoagulants.	☐	X ☐
__ Active peptic ulcer or g.i. hemorrhage.	☐	X ☐
__ Significant liver or kidney disease.	☐	X ☐
__ Hemopoietic disorders.	☐	X ☐

If none of these conditions applies to the patient, he or she may enter the study and receive test medication + instructions for use.

Start of treatment at onset of pain. DENTAL SURGERY FORM C

Diflunisal versus control

Investigator: Dr.M.L. McCUE

Name or initials: J.L. Study nr: 75

MEDICATION (please record times in 0-24 hours)

Test medication:

first dose was taken at	1300 hour on day of surgery				
second dose was taken at	1700 hour on day of surgery	X ☐	*/ day after surgery	☐	
third dose was taken at	2100	-	X ☐	-	☐
fourth dose was taken at	1000	-	☐	-	X ☐
fifth dose was taken at	.....	-	☐	-	☐

If not all doses were used, give reason: _____

Did patient take any other analgesic since surgery? X No ; Yes

If yes, name of drug: _____ Dose: _____

Time first dose was taken: _____

Did patient take strong alcoholic beverages X No Yes If yes, specify number of glasses: _____

Did patient use drugs for other diseases X No Yes If yes, specify: _____ (name + dose) _____

FIGURE 93

DENTAL SURGERY FORM B

Start of treatment at onset of pain.
Diflunisal versus control
Name of investigator: Dr. M.L. McCUE

Name or initials: J. L. Study nr: 75

CONTROL VISIT Evaluation on of day after surgery date: oct. 5 hour: 1800
Only to be filled in if patient took test medication.

1. PATIENTS EVALUATION

Parameters	At intake of first dose of test medication	At control visit	Description of rating scales on opposite page.
1. Pain	1	0	
11. Patient's opinion on treatment efficacy		2	

11. ADVERSE REACTIONS

XX None, or specify below:	Maximal intensity	Seriousness	Drug relationship	Action taken if any
Adverse reaction codes:	1 = mild 2 = moderate 3 = severe	1=not serious 2=serious	1=definitely not 2=probably not 3=possibly 4=probably 5=definitely	(e.g. dose reduction or discontinuation of test drug)

If adverse reaction was still present at control visit, give outcome if known (mandatory for serious reactions):

completely recovered
residual effects
reaction still present
died

patient receives treatment for reaction: yes; no
if yes, specify: _____

11. Investigator's overall evaluation taking into account expected spontaneous course of symptoms for individual patient.

Adverse reactions	Efficacy → None	Poor	Fair	Good	Excellent
No adverse reactions	0		X		
Acceptable adverse reactions					
Unacceptable adverse reactions					

Comments, if any: _____

FIGURE 94

Start of treatment at onset of pain. DENTAL SURGERY FORM A

Diflunisal versus control

To be completed on day of surgery

Name or Initials: A.W.	Age: 49 yrs.	Sex: M F	Study nr: 76

Procedure: Removal of impacted tooth Impacted element: 18, 48.

Additional surgery, if any: none

Date of surgery: oct. 4 time am. Degree of trauma: mild ☐ moderate ☒X severe ☐

Anesthesia given: local anaesth. and I.V. sedation

Exclusion criteria for participation in the study

Please check all items:

	YES	NO
__ Age below legal consent or over 70 years.	☐	☒
__ Confirmed pregnancy or a practical possibility of pregnancy	☐	☒
__ Hypersensitivity to salicylates or to the control medication	☐	☒
__ Current treatment with: systemic corticosteroid or anticoagulants.	☐	☒
__ Active peptic ulcer or g.i. hemorrhage.	☐	☒
__ Significant liver or kidney disease.	☐	☒
__ Hemopoietic disorders.	☐	☒

If none of these conditions applies to the patient, he or she may enter the study and receive test medication + instructions for use.

Start of treatment at onset of pain. DENTAL SURGERY FORM C

Diflunisal versus control

Investigator: Dr. M.L. McCUE

Name or initials: A.W. Study nr: 76

MEDICATION (please record times in 0-24 hours)

Test medication:

first dose was taken at 1220 ...hour on day of surgery

second dose was taken at 1820 ....hour on day of surgery ☐ XX / day after surgery ☐

third dose was taken at 0900 - ☐ - ☒

fourth dose was taken at ..... - ☐ - ☐

fifth dose was taken at ..... - ☐ - ☐

If not all doses were used, give reason:

Did patient take any other analgesic since surgery? No X ; Yes

If yes, name of drug: Dose:

Time first dose was taken:

Did patient take strong alcoholic beverages No X Yes If yes, specify number of glasses:

Did patient use drugs for other diseases No X Yes If yes, specify: ?? (name + dose)

FIGURE 95

DENTAL SURGERY FORM B

Start of treatment at onset of pain.

Diflunisal versus control

Name of investigator: Dr. M.L. McCUE

Name or initials: A.W. Study nr: 76

CONTROL VISIT Evaluation on of day after surgery date: oct. 5 hour: 1100
Only to be filled in if patient took test medication.

1. PATIENTS EVALUATION

Parameters	At intake of first dose of test medication	At control visit	Description of rating scales on opposite page
1. Pain	1	2	
11. Patient's opinion on treatment efficacy		3	

11. ADVERSE REACTIONS

Nxxex or specify below:	Maximal intensity	Seriousness	Drug relationship	Action taken if any
Adverse reaction codes:	1 = mild 2 = moderate 3 = severe	1=not serious 2=serious	1=definitely not 2=probably not 3=possibly 4=probably 5=definitely	(e.g. dose reduction or discontinuation of test drug)

If adverse reaction was still present at control visit, give outcome if known (mandatory for serious reactions):

completely recovered
residual effects
reaction still present
died

patient receives treatment for reaction: yes; no
if yes, specify:

11. Investigator's overall evaluation taking into account expected spontaneous course of symptoms for individual patient.

Adverse reactions ↓ Efficacy →	None	Poor	Fair	Good	Excellent
No adverse reactions 0				x	
Acceptable adverse reactions					
Unacceptable adverse reactions					

Comments, if any:

FIGURE 96

Start of treatment at onset of pain. DENTAL SURGERY FORM A

Diflunisal versus control

To be completed on day of surgery

Name or Initials: B.D.	Age: 22 yrs.	Sex: M F	Study nr: 77

Procedure: Removal of impacted tooth Impacted element: 38

Additional surgery, if any: none

Date of surgery: oct.4 time p.m. Degree of trauma: mild XX
moderate ☐
severe ☐

Anesthesia given: local anaesth. and I.V. sedation

Exclusion criteria for participation in the study

Please check all items:

	YES	NO
__ Age below legal consent or over 70 years.	☐	X ☐
__ Confirmed pregnancy or a practical possibility of pregnancy	☐	X ☐
__ Hypersensitivity to salicylates or to the control medication	☐	X ☐
__ Current treatment with: systemic corticosteroid or anticoagulants.	☐	X ☐
__ Active peptic ulcer or g.i. hemorrhage.	☐	X ☐
__ Significant liver or kidney disease.	☐	X ☐
__ Hemopoietic disorders.	☐	X ☐

If none of these conditions applies to the patient, he or she may enter the study and receive test medication + instructions for use.

Start of treatment at onset of pain. DENTAL SURGERY FORM C

Diflunisal versus control

Investigator: Dr. M.L. McCUE

Name or initials: B.D. Study nr: 77

MEDICATION (please record times in 0-24 hours)

Test medication:

first dose was taken at .....hour on day of surgery

second dose was taken at .....hour on day of surgery ☐ */ day after surgery ☐

third dose was taken at ..... - ☐ - ☐

fourth dose was taken at ..... - ☐ - ☐

fifth dose was taken at ..... - ☐ - ☐

If not all doses were used, give reason: _____

Did patient take any other analgesic since surgery? No ; Yes

If yes, name of drug: _____ Dose: _____

Time first dose was taken: _____

Did patient take strong alcoholic beverages No Yes If yes, specify number of glasses: __

Did patient use drugs for other diseases No Yes If yes, specify: _____

(name + dose) _____

FIGURE 97

DENTAL SURGERY FORM B

Start of treatment at onset of pain.

Diflunisal versus control

Dr. M. L. MCCUE

Name of investigator:

Name or initials: B.D. Study nr: 77

CONTROL VISIT Evaluation on of day after surgery date: hour:
Only to be filled in if patient took test medication.

1. PATIENTS EVALUATION

Parameters	At intake of first dose of test medication	At control visit	Description of rating scales on opposite page.
1. Pain			
11. Patient's opinion on treatment efficacy			

11. ADVERSE REACTIONS

None, or specify below:	Maximal intensity	Seriousness	Drug relationship	Action taken if any
Adverse reaction codes:	1 = mild 2 = moderate 3 = severe	1=not serious 2=serious	1=definitely not 2=probably not 3=possibly 4=probably 5=definitely	(e.g. dose reduction or discontinuation of test drug)

If adverse reaction was still present at control visit, give outcome if known (mandatory for serious reactions):

completely recovered
residual effects
reaction still present
died

patient receives treatment for reaction: yes; no
if yes, specify:

11. Investigator's overall evaluation taking into account expected spontaneous course of symptoms for individual patient.

Adverse reactions Efficacy →	None	Poor	Fair	Good	Excellent
No adverse reactions					
Acceptable adverse reactions					
Unacceptable adverse reactions					

Comments, if any: unable to contact the patient

FIGURE 98

Start of treatment at onset of pain. DENTAL SURGERY FORM A

Diflunisal versus control

To be completed on day of surgery

Name or Initials: L.C.	Age: 20 yrs.	Sex: F (M / F)	Study nr: 78

Procedure: Removal of impacted tooth Impacted element: 18, 38.

Additional surgery, if any: 28

Date of surgery: oct.4 time a.m. Degree of trauma: mild ☐ moderate X ☐ severe ☐

Anesthesia given: local anesth. and I.V. sedation

Exclusion criteria for participation in the study

Please check all items:

	YES	NO
__ Age below legal consent or over 78 years.	☐	X ☐
__ Confirmed pregnancy or a practical possibility of pregnancy	☐	X ☐
__ Hypersensitivity to salicylates or to the control medication	☐	X ☐
__ Current treatment with: systemic corticosteroid or anticoagulants.	☐	X ☐
__ Active peptic ulcer or g.i. hemorrhage.	☐	X ☐
__ Significant liver or kidney disease.	☐	X ☐
__ Hemopoietic disorders.	☐	X ☐

If none of these conditions applies to the patient, he or she may enter the study and receive test medication + instructions for use.

Start of treatment at onset of pain. DENTAL SURGERY FORM C

Diflunisal versus control

Investigator: DR. M.L. McCUE

Name or initials: L.C. Study nr: 78

MEDICATION (please record times in 0-24 hours)

Test medication:

first dose was taken at 1330 hour on day of surgery

second dose was taken at .....hour on day of surgery ☐ */ day after surgery ☐

third dose was taken at ..... = ☐ = ☐

fourth dose was taken at ..... = ☐ = ☐

fifth dose was taken at ..... = ☐ = ☐

If not all doses were used, give reason: continue did not with the study because the medication did not work

Did patient take any other analgesic since surgery? No ; Yes XX

If yes, name of drug: 292 Dose: 2 tabs

Time first dose was taken: 1800 oct. 4

Did patient take strong alcoholic beverages? No Yes If yes, specify number of glasses:

Did patient use drugs for other diseases? No Yes If yes, specify: (name + dose)

FIGURE 99

DENTAL SURGERY FORM B

Start of treatment at onset of pain.

Diflunisal versus control

Name of investigator: Dr. M.L. McCUE

Name or initials: L.C. Study nr: 78

CONTROL VISIT Evaluation on of day after surgery date: oct. 5 hour: 1200
Only to be filled in if patient took test medication.

1. PATIENTS EVALUATION

Parameters	At intake of first dose of test medication	At control visit	Description of rating scales on opposite page.
1. Pain	3	3	
11. Patient's opinion on treatment efficacy		0	

11. ADVERSE REACTIONS

XX None, or specify below:	Maximal intensity	Seriousness	Drug relationship	Action taken if any
Adverse reaction codes:	1 = mild 2 = moderate 3 = severe	1=not serious 2=serious	1=definitely not 2=probably not 3=possibly 4=probably 5=definitely	(e.g. dose reduction or discontinuation of test drug)

If adverse reaction was still present at control visit, give outcome if known (mandatory for serious reactions):

completely recovered
residual effects
reaction still present
died

patient receives treatment for reaction: yes; no
if yes, specify:

11. Investigator's overall evaluation taking into account expected spontaneous course of symptoms for individual patient.

Adverse reactions	Efficacy → None	Poor	Fair	Good	Excellent
No adverse reactions	0 x				
Acceptable adverse reactions					
Unacceptable adverse reactions					

Comments, if any: patient received no relief from the first dose and discontinued the study

FIGURE 100

Start of treatment at onset of pain. DENTAL SURGERY FORM A

Diflunisal versus control

To be completed on day of surgery

Name or Initials: L.S.	Age: 22 yrs.	Sex: F M	Study nr: 79

Procedure: Removal of impacted tooth Impacted element: 18, 28, 38, 48

Additional surgery, if any: none

Date of surgery: oct.4 time 8 am. Degree of trauma: mild ☐ moderate ☒ severe ☐

Anesthesia given: general

Exclusion criteria for participation in the study

Please check all items:

	YES	NO
__ Age below legal consent or over 70 years.	☐	☒
__ Confirmed pregnancy or a practical possibility of pregnancy	☐	☒
__ Hypersensitivity to salicylates or to the control medication	☐	☒
__ Current treatment with: systemic corticosteroid or anticoagulants.	☐	☒
__ Active peptic ulcer or g.i. hemorrhage.	☐	☒
__ Significant liver or kidney disease.	☐	☒
__ Hemopoietic disorders.	☐	☒

If none of these conditions applies to the patient, he or she may enter the study and receive test medication + instructions for use.

Start of treatment at onset of pain. DENTAL SURGERY FORM C

Diflunisal versus control

Investigator: Dr. M.L. McCUE

Name or initials: L.S. Study nr: 79

MEDICATION (please record times in 0-24 hours)

Test medication:

first dose was taken at 1300 hour on day of surgery

second dose was taken at 1700 hour on day of surgery ☒ */ day after surgery ☐

third dose was taken at	2100	-	☒	-	☐
fourth dose was taken at	0730	-	☐	-	☒
fifth dose was taken at	.....	-	☐	-	☐

If not all doses were used, give reason:

Did patient take any other analgesic since surgery? ☒ : Yes

If yes, name of drug: Dose:

Time first dose was taken:

Did patient take strong alcoholic beverages ☒ Yes : If yes, specify number of glasses:

Did patient use drugs for other diseases ☒ Yes If yes, specify:

(name + dose)

FIGURE 101

DENTAL SURGERY FORM B

Start of treatment at onset of pain. Diflunisal versus control

Name of investigator: Dr. M.L. McCUE

Name or initials: L.S. Study nr: 79

CONTROL VISIT Evaluation on of day after surgery date: oct. 6 hour: 1200
Only to be filled in if patient took test medication.

1. PATIENTS EVALUATION

Parameters	At intake of first dose of test medication	At control visit	Description of rating scales on opposite page.
1. Pain	3	2	
11. Patient's opinion on treatment efficacy		1	

11. ADVERSE REACTIONS

XX None, or specify below:	Maximal intensity	Seriousness	Drug relationship	Action taken if any
Adverse reaction codes:	1 = mild 2 = moderate 3 = severe	1=not serious 2=serious	1=definitely not 2=probably not 3=possibly 4=probably 5=definitely	(e.g. dose reduction or discontinuation of test drug)

If adverse reaction was still present at control visit, give outcome if known (mandatory for serious reactions):

completely recovered
residual effects
reaction still present
died

patient receives treatment for reaction: yes; no
if yes, specify:

11. Investigator's overall evaluation taking into account expected spontaneous course of symptoms for individual patient.

Adverse reactions	Efficacy →	None	Poor	Fair	Good	Excellent
No adverse reactions	0		X			
Acceptable adverse reactions						
Unacceptable adverse reactions						

Comments, if any: patient had no relief from the first two doses and only slightly from the last two doses

FIGURE 102

Start of treatment at onset of pain. DENTAL SURGERY FORM A

Diflunisal versus control

To be completed on day of surgery

Name or Initials: P.T.	Age 20 yrs.	Sex: M / F	Study nr: 80

Procedure: Removal of impacted tooth Impacted element: 18, 28, 38, 48.

Additional surgery, if any: none

Date of surgery: oct.4 time 4 PM. Degree of trauma: mild ☐ moderate ☒ severe ☐

Anesthesia given: general

Exclusion criteria for participation in the study

Please check all items:

	YES	NO
__ Age below legal consent or over 70 years.	☐	☒
__ Confirmed pregnancy or a practical possibility of pregnancy	☐	☒
__ Hypersensitivity to salicylates or to the control medication	☐	☒
__ Current treatment with: systemic corticosteroid or anticoagulants.	☐	☒
__ Active peptic ulcer or g.i. hemorrhage.	☐	☒
__ Significant liver or kidney disease.	☐	☒
__ Hemopoietic disorders.	☐	☒

If none of these conditions applies to the patient, he or she may enter the study and receive test medication + instructions for use.

Start of treatment at onset of pain. DENTAL SURGERY FORM C

Diflunisal versus control

Investigator: Dr.M.L. McCOL

Name or initials: P.T. Study nr: 80

MEDICATION (please record times in 0-24 hours)

Test medication:

first dose was taken at 1230 hour on day of surgery

second dose was taken at 1830 hour on day of surgery ☒ */ day after surgery ☐

third dose was taken at ..... - ☐ - ☐

fourth dose was taken at ..... - ☐ - ☐

fifth dose was taken at ..... - ☐ - ☐

If not all doses were used, give reason: nauses and vomitting after the second dose

Did patient take any other analgesic since surgery? ☒ No ; Yes

If yes, name of drug: Dose:

Time first dose was taken:

Did patient take strong alcoholic beverages ☒ No Yes If yes, specify number of glasses:

Did patient use drugs for other diseases ☒ No Yes If yes, specify: (name + dose)

FIGURE 103

DENTAL SURGERY FORM B

Start of treatment at onset of pain.

Diflunisal versus control

Name of investigator: Dr. M.L. McCUE

Name or initials: P.T. Study nr: 80

CONTROL VISIT Evaluation on of day after surgery date: oct.6 hour: 1230
Only to be filled in if patient took test medication.

1. PATIENTS EVALUATION

Parameters	At intake of first dose of test medication	At control visit	Description of rating scales on opposite page.
1. Pain	2	0	
11. Patient's opinion on treatment efficacy		3	

11. ADVERSE REACTIONS

None, or specify below:	Maximal intensity	Seriousness	Drug relationship	Action taken if any
nausea and vomitting	1	1	3	disc. medication
Adverse reaction codes:	1 = mild 2 = moderate 3 = severe	1=not serious 2=serious	1=definitely not 2=probably not 3=possibly 4=probably 5=definitely	(e.g. dose reduction or discontinuation of test drug)

If adverse reaction was still present at control visit, give outcome if known (mandatory for serious reactions):

completely recovered
residual effects
reaction still present
died

patient receives treatment for reaction: yes; no
if yes, specify:

11. Investigator's overall evaluation taking into account expected spontaneous course of symptoms for individual patient.

Adverse reactions Efficacy →	None	Poor	Fair	Good	Excellent
No adverse reactions					
Acceptable adverse reactions 1				x	
Unacceptable adverse reactions					

Comments, if any: patient discontinued medication after nausea and vomitting. The medication was effective while being taken

FIGURE 104

Start of treatment at onset of pain. DENTAL SURGERY FORM A

Diflunisal versus control

To be completed on day of surgery

Name or Initials: H.H.	Age: 31 yrs.	Sex: M X F	Study nr: 81

Procedure: Removal of impacted tooth Impacted element: 18, 28, 38, 48.

Additional surgery, if any: none

Date of surgery: oct.4 time 8 a.m. Degree of trauma: mild ☐ moderate ☐ severe X

Anesthesia given: general

Exclusion criteria for participation in the study

Please check all items:

	YES	NO
__ Age below legal consent or over 70 years.	☐	X
__ Confirmed pregnancy or a practical possibility of pregnancy	☐	X
__ Hypersensitivity to salicylates or to the control medication	☐	X
__ Current treatment with: systemic corticosteroid or anticoagulants.	☐	X
__ Active peptic ulcer or g.i. hemorrhage.	☐	X
__ Significant liver or kidney disease.	☐	X
__ Hemopoietic disorders.	☐	X

If none of these conditions applies to the patient, he or she may enter the study and receive test medication → instructions for use.

Start of treatment at onset of pain. DENTAL SURGERY FORM C

Diflunisal versus control

Investigator: Dr.M.L. McCUE

Name or initials: H.H. Study nr: 81

MEDICATION (please record times in 0-24 hours)

Test medication:

first dose was taken at 1000 ....hour on day of surgery

second dose was taken at 1800 .....hour on day of surgery X ☐ */ day after surgery ☐

third dose was taken at ..... - ☐ - ☐

fourth dose was taken at ..... - ☐ - ☐

fifth dose was taken at ..... - ☐ - ☐

If not all doses were used, give reason: did not require further medication

Did patient take any other analgesic since surgery? No X ; Yes

If yes, name of drug: Dose:

Time first dose was taken:

Did patient take strong alcoholic beverages? No XX Yes If yes, specify number of glasses:

Did patient use drugs for other diseases XX No Yes If yes, specify: (name + dose)

FIGURE 105

DENTAL SURGERY FORM B

Start of treatment at onset of pain.

Diflunisal versus control

Name of investigator: Dr.M.L. MCCUE

Name or initials: H.H. Study nr: 81

CONTROL VISIT Evaluation on of day after surgery date: oct. 6 hour 1200

Only to be filled in if patient took test medication.

1. PATIENTS EVALUATION

Parameters	At intake of first dose of test medication	At control visit	Description of rating scales on opposite page.
1. Pain	1	0	
11. Patient's opinion on treatment efficacy		3	

11. ADVERSE REACTIONS

None or specify below:	Maximal intensity	Seriousness	Drug relationship	Action taken if any
Adverse reaction codes:	1 = mild 2 = moderate 3 = severe	1=not serious 2=serious	1=definitely not 2=probably not 3=possibly 4=probably 5=definitely	(e.g. dose reduction or discontinuation of test drug)

If adverse reaction was still present at control visit, give outcome if known (mandatory for serious reactions):

completely recovered
residual effects
reaction still present
died

patient receives treatment for reaction: yes; no
if yes, specify: _____

11. Investigator's overall evaluation taking into account expected spontaneous course of symptoms for individual patient.

Adverse reactions Efficacy →	None	Poor	Fair	Good	Excellent
No adverse reactions ↓ 0				X	
Acceptable adverse reactions					
Unacceptable adverse reactions					

Comments, if any: patient did feel much pain but the medication was effective in relieving any pain present

FIGURE 106

Start of treatment at onset of pain. DENTAL SURGERY FORM A

Diflunisal versus control

To be completed on day of surgery

Name or Initials: S.H.	Age: 18 yrs.	Sex: M / F	Study nr: 82

Procedure: Removal of impacted tooth Impacted element: 18, 28, 38, 48.

Additional surgery, if any: none

Date of surgery: oct.5 time a.m. Degree of trauma: mild ☐ moderate ☒ severe ☐

Anesthesia given: general

Exclusion criteria for participation in the study

Please check all items:

	YES	NO
__ Age below legal consent or over 70 years.	☐	☒
__ Confirmed pregnancy or a practical possibility of pregnancy	☐	☒
__ Hypersensitivity to salicylates or to the control medication	☐	☒
__ Current treatment with: systemic corticosteroid or anticoagulants.	☐	☒
__ Active peptic ulcer or g.i. hemorrhage.	☐	☒
__ Significant liver or kidney disease.	☐	☒
__ Hemopoietic disorders.	☐	☒

If none of these conditions applies to the patient, he or she may enter the study and receive test medication + instructions for use.

Start of treatment at onset of pain. DENTAL SURGERY FORM C

Diflunisal versus control

Investigator: Dr. M.L. McCUE

Name or initials: S.H. Study nr: 82

MEDICATION (please record times in 0-24 hours)

Test medication:

first dose was taken at 1200 hour on day of surgery

second dose was taken at 2030 hour on day of surgery ☐ / day after surgery ☐

third dose was taken at	- ☐	- ☐		
fourth dose was taken at	- ☐	- ☐		
fifth dose was taken at	- ☐	- ☐		

If not all doses were used, give reason: no further medication required

Did patient take any other analgesic since surgery? NO ; Yes

If yes, name of drug: Dose:

Time first dose was taken:

Did patient take strong alcoholic beverages NO Yes If yes, specify number of glasses:

Did patient use drugs for other diseases NO Yes If yes, specify: (name + dose)

FIGURE 107

DENTAL SURGERY FORM B

Start of treatment at onset of pain.
Diflunisal versus control
Dr. M.L. MCCUE
Name of investigator:

Name or initials: S.H. Study nr: 82

CONTROL VISIT Evaluation on of day after surgery date: oct.6 hour: 1230
Only to be filled in if patient took test medication.

1. PATIENTS EVALUATION

Parameters	At intake of first dose of test medication	At control visit	Description of rating scales on opposite page.
1. Pain	4	1	
11. Patient's opinion on treatment efficacy		4	

11. ADVERSE REACTIONS

XX None, or specify below:	Maximal intensity	Seriousness	Drug relationship	Action taken if any
Adverse reaction codes:	1 = mild 2 = moderate 3 = severe	1=not serious 2=serious	1=definitely not 2=probably not 3=possibly 4=probably 5=definitely	(e.g. dose reduction or discontinuation of test drug)

If adverse reaction was still present at control visit, give outcome if known (mandatory for serious reactions):

completely recovered
residual effects
reaction still present
died

patient receives treatment for reaction: yes; no
if yes, specify:

11. Investigator's overall evaluation taking into account expected spontaneous course of symptoms for individual patient.

Adverse reactions	Efficacy → None	Poor	Fair	Good	Excellent
No adverse reactions	0				X
Acceptable adverse reactions					
Unacceptable adverse reactions					

Comments, if any: patient was happy with the medication

FIGURE 108

Start of treatment at onset of pain. DENTAL SURGERY FORM A

Diflunisal versus control

To be completed on day of surgery

Name or Initials: V.A.	Age: 21 yrs.	Sex: M X F	Study nr: 83

Procedure: Removal of impacted tooth Impacted element: ~~18, 28, 38, 48~~.

Additional surgery, if any: none

Date of surgery: oct.5 time: am. Degree of trauma: mild ☐ moderate X ☒ severe ☐

Anesthesia given: general

Exclusion criteria for participation in the study

Please check all items:

	YES	NO
__ Age below legal consent or over 70 years.	☐	X ☒
__ Confirmed pregnancy or a practical possibility of pregnancy	☐	X ☒
__ Hypersensitivity to salicylates or to the control medication	☐	X ☒
__ Current treatment with: systemic corticosteroid or anticoagulants.	☐	X ☒
__ Active peptic ulcer or g.i. hemorrhage.	☐	X ☒
__ Significant liver or kidney disease.	☐	X ☒
__ Hemopoietic disorders.	☐	X ☒

If none of these conditions applies to the patient, he or she may enter the study and receive test medication + instructions for use.

Start of treatment at onset of pain. DENTAL SURGERY FORM C

Diflunisal versus control

Investigator: Dr.M.L. McCUE

Name or initials: V.A. Study nr: 83

MEDICATION (please record times in 0-24 hours)

Test medication:

first dose was taken at 1330 hour on day of surgery

second dose was taken at 1930 hour on day of surgery ☐ */ day after surgery ☐

third dose was taken at 0730 ..... - ☐ - X ☒

fourth dose was taken at ..... - ☐ - ☐

fifth dose was taken at ..... - ☐ - ☐

If not all doses were used, give reason: _____

Did patient take any other analgesic since surgery? X ☒ No ; ☐ Yes

If yes, name of drug: _____ Dose: _____

Time first dose was taken: _____

Did patient take strong alcoholic beverages X ☒ No ☐ Yes If yes, specify number of glasses: _____

Did patient use drugs for other diseases X ☒ No ☐ Yes If yes, specify: _____

(name + dose) _____

FIGURE 109

DENTAL SURGERY FORM B

Start of treatment at onset of pain.

Diflunisal versus control

Name of investigator: Dr. M.L. MCCUE

Name or initials: V.A. Study nr: 83

CONTROL VISIT Evaluation on of day after surgery date: oct.6 hour: 1800
Only to be filled in if patient took test medication.

1. PATIENTS EVALUATION

Parameters	At intake of first dose of test medication	At control visit	Description of rating scales on opposite page.
1. Pain	3	1	
11. Patient's opinion on treatment efficacy		3	

11. ADVERSE REACTIONS

None, or specify below:	Maximal intensity	Seriousness	Drug relationship	Action taken if any
nausea ,diarrhoea	1	1	2	none
~~vomitting~~				
Adverse reaction codes:	1 = mild 2 = moderate 3 = severe	1=not serious 2=serious	1=definitely not 2=probably not 3=possibly 4=probably 5=definitely	(e.g. dose reduction or discontinuation of test drug)

If adverse reaction was still present at control visit, give outcome if known (mandatory for serious reactions):

completely recovered
residual effects
reaction still present
died

patient receives treatment for reaction: yes; no
if yes, specify:

11. Investigator's overall evaluation taking into account expected spontaneous course of symptoms for individual patient.

Adverse reactions Efficacy →	None	Poor	Fair	Good	Excellent
No adverse reactions					
Acceptable adverse reactions 1				x	
Unacceptable adverse reactions					

Comments, if any: symptoms possibly due to general anesthesia

FIGURE 110

Start of treatment at onset of pain. DENTAL SURGERY FORM A

Diflunisal versus control

To be completed on day of surgery

Name or Initials: P.V.	Age: 28 yrs.	Sex: M X F	Study nr: 84

Procedure: Removal of impacted tooth Impacted element: 48.

Additional surgery, if any: 18, 28.

Date of surgery: oct. 5 time 8 AM. Degree of trauma: mild ☐ moderate ☒ severe ☐

Anesthesia given: general

Exclusion criteria for participation in the study

Please check all items:

	YES	NO
__ Age below legal consent or over 70 years.	☐	X ☐
__ Confirmed pregnancy or a practical possibility of pregnancy	☐	X ☐
__ Hypersensitivity to salicylates or to the control medication	☐	X ☐
__ Current treatment with: systemic corticosteroid or anticoagulants.	☐	X ☐
__ Active peptic ulcer or g.i. hemorrhage.	☐	X ☐
__ Significant liver or kidney disease.	☐	X ☐
__ Hemopoietic disorders.	☐	X ☐

If none of these conditions applies to the patient, he or she may enter the study and receive test medication + instructions for use.

Start of treatment at onset of pain. DENTAL SURGERY FORM C

Diflunisal versus control

Investigator: Dr. M.L. McCUE

Name or initials: P.V. Study nr: 84

MEDICATION (please record times in 0-24 hours)

Test medication:

first dose was taken at 2100 hour on day of surgery

second dose was taken at 0400 hour on day of surgery ☐ */ day after surgery XX ☐

third dose was taken at ..... = ☐ = ☐

fourth dose was taken at ..... = ☐ = ☐

fifth dose was taken at ..... = ☐ = ☐

If not all doses were used, give reason: two doses were sufficient to relieve pain

Did patient take any other analgesic since surgery? No ; Yes

If yes, name of drug: Dose:

Time first dose was taken:

Did patient take strong alcoholic beverages XX Yes If yes, specify number of glasses:

Did patient use drugs for other diseases XX Yes If yes, specify:

(name + dose)

FIGURE III

DENTAL SURGERY FORM B

Start of treatment at onset of pain.
Diflunisal versus control

Name of investigator: Dr. M. L. McCUE

Name or initials: P.V. Study nr: 84

CONTROL VISIT Evaluation on of day after surgery date: oct. 6 hour: 1900
Only to be filled in if patient took test medication.

1. PATIENTS EVALUATION

Parameters	At intake of first dose of test medication	At control visit	Description of rating scales on opposite page.
1. Pain	2	0	
11. Patient's opinion on treatment efficacy		3	

11. ADVERSE REACTIONS

None, or specify below:	Maximal intensity	Seriousness	Drug relationship	Action taken if any
	1	1	3	none
diarrhoea, slight				
headache				
Adverse reaction codes:	1 = mild 2 = moderate 3 = severe	1=not serious 2=serious	1=definitely not 2=probably not 3=possibly 4=probably 5=definitely	(e.g. dose reduction or discontinuation of test drug)

If adverse reaction was still present at control visit, give outcome if known (mandatory for serious reactions):

completely recovered
residual effects
reaction still present
died

patient receives treatment for reaction: yes; no
if yes, specify: _____

11. Investigator's overall evaluation taking into account expected spontaneous course of symptoms for individual patient.

Adverse reactions ↓ Efficacy →	None	Poor	Fair	Good	Excellent
No adverse reactions					
Acceptable adverse reactions 1				x	
Unacceptable adverse reactions					

Comments, if any: adverse symptoms may be due to general anesthesia

FIGURE 112

Start of treatment at onset of pain. DENTAL SURGERY FORM A

Diflunisal versus control

To be completed on day of surgery

Name or Initials: W.H.	Age: 23 yrs.	Sex: M X F	Study nr: 85

Procedure: Removal of impacted tooth Impacted element: 18, 28.

Additional surgery, if any: apicoectomy 11,21.

Date of surgery: oct. 5 Time: a.m. Degree of trauma: mild ☐ moderate ☒ severe ☐

Anesthesia given: general

Exclusion criteria for participation in the study

Please check all items:

	YES	NO
__ Age below legal consent or over 70 years.	☐	☒
__ Confirmed pregnancy or a practical possibility of pregnancy	☐	☒
__ Hypersensitivity to salicylates or to the control medication	☐	☒
__ Current treatment with: systemic corticosteroid or anticoagulants.	☐	☒
__ Active peptic ulcer or g.i. hemorrhage.	☐	☒
__ Significant liver or kidney disease.	☐	☒
__ Hemopoietic disorders.	☐	☒

If none of these conditions applies to the patient, he or she may enter the study and receive test medication + instructions for use.

Start of treatment at onset of pain. DENTAL SURGERY FORM C

Diflunisal versus control

Investigator: Dr. M.L. MCCUE

Name or Initials: W.H. Study nr: 85

MEDICATION (please record times in 0-24 hours)

Test medication:

first dose was taken at 2000 hour on day of surgery

second dose was taken at 0800 hour on day of surgery ☐ */ day after surgery ☒

third dose was taken at ..... - ☐ - ☐

fourth dose was taken at ..... - ☐ - ☐

fifth dose was taken at ..... - ☐ - ☐

If not all doses were used, give reason: only two doses were required for pain

Did patient take any other analgesic since surgery? NO ; Yes

If yes, name of drug: Dose:

Time first dose was taken:

Did patient take strong alcoholic beverages ☒ No Yes If yes, specify number of glasses:

Did patient use drugs for other diseases ☒ No Yes If yes, specify: (name + dose)

FIGURE 113

DENTAL SURGERY FORM B

Start of treatment at onset of pain.
Diflunisal versus control

Name of investigator: Dr. M.L. McCUE

Name or initials: W.H. Study nr: 85

CONTROL VISIT Evaluation on of day after surgery date: Oct 6 hour: 1300
Only to be filled in if patient took test medication.

1. PATIENTS EVALUATION

Parameters	At intake of first dose of test medication	At control visit	Description of rating scales on opposite page.
1. Pain	4	1	
11. Patient's opinion on treatment efficacy		4	

11. ADVERSE REACTIONS

~~XXXX~~or specify below:	Maximal intensity	Seriousness	Drug relationship	Action taken if any
Adverse reaction codes:	1 = mild 2 = moderate 3 = severe	1=not serious 2=serious	1=definitely not 2=probably not 3=possibly 4=probably 5=definitely	(e.g. dose reduction or discontinuation of test drug)

If adverse reaction was still present at control visit, give outcome if known (mandatory for serious reactions):

completely recovered
residual effects
reaction still present
died

patient receives treatment for reaction: yes; no
if yes, specify:

11. Investigator's overall evaluation taking into account expected spontaneous course of symptoms for individual patient.

Adverse reactions	Efficacy →	None	Poor	Fair	Good	Excellent
No adverse reactions	0					x
Acceptable adverse reactions						
Unacceptable adverse reactions						

Comments, if any: patient was happy with the medication

FIGURE 114

Start of treatment at onset of pain. DENTAL SURGERY FORM A

Diflunisal versus control

To be completed on day of surgery

Name or Initials: K.F.	Age: 24 yrs.	Sex: M F	Study nr: 86

Procedure: Removal of impacted tooth Impacted element: 18, 28, 38, 48

Additional surgery, if any: none

Date of surgery: oct. 5 time 8 a.m. Degree of trauma: mild ☐ moderate ☐ very severe ☒

Anesthesia given: general

Exclusion criteria for participation in the study

Please check all items:

	YES	NO
__ Age below legal consent or over 70 years.	☐	☒
__ Confirmed pregnancy or a practical possibility of pregnancy	☐	☒
__ Hypersensitivity to salicylates or to the control medication	☐	☒
__ Current treatment with: systemic corticosteroid or anticoagulants.	☐	☒
__ Active peptic ulcer or g.i. hemorrhage.	☐	☒
__ Significant liver or kidney disease.	☐	☒
__ Hemopoietic disorders.	☐	☒

If none of these conditions applies to the patient, he or she may enter the study and receive test medication + instructions for use.

Start of treatment at onset of pain. DENTAL SURGERY FORM C

Diflunisal versus control

Investigator: Dr. M.L. MCCUE

Name or Initials: K.F. Study nr: 86

MEDICATION (please record times in 0-24 hours)

Test medication:

first dose was taken at 1800 hour on day of surgery

second dose was taken at 0800 hour on day of surgery ☐ */ day after surgery ☒

third dose was taken at ..... - ☐ - ☐

fourth dose was taken at ..... - ☐ - ☐

fifth dose was taken at ..... - ☐ - ☐

If not all doses were used, give reason: no further dose required but patient took a 292 24 hrs. after surgery

Did patient take any other analgesic since surgery? No ; Yes

If yes, name of drug: 292 Dose: 2 tabs

Time first dose was taken: 1500 hrs. oct 6

Did patient take strong alcoholic beverages? No X Yes If yes, specify number of glasses:

Did patient use drugs for other diseases X No Yes If yes, specify: (name + dose)

FIGURE 115

DENTAL SURGERY FORM B

Start of treatment at onset of pain.

Diflunisal versus control

Name of investigator: Dr. M.L. MCCUE

Name or initials: K.F. Study nr: 86

CONTROL VISIT Evaluation on of day after surgery date: oct. 6 hour: 1200
Only to be filled in if patient took test medication.

1. PATIENTS EVALUATION

Parameters	At intake of first dose of test medication	At control visit	Description of rating scales on opposite page.
1. Pain	4	0	
11. Patient's opinion on treatment efficacy		2	

11. ADVERSE REACTIONS

None, or specify below: X	Maximal intensity	Seriousness	Drug relationship	Action taken if any
Adverse reaction codes:	1 = mild 2 = moderate 3 = severe	1=not serious 2=serious	1=definitely not 2=probably not 3=possibly 4=probably 5=definitely	(e.g. dose reduction or discontinuation of test drug)

If adverse reaction was still present at control visit, give outcome if known (mandatory for serious reactions):

completely recovered
residual effects
reaction still present
died

patient receives treatment for reaction: yes; no
if yes, specify:

11. Investigator's overall evaluation taking into account expected spontaneous course of symptoms for individual patient.

Adverse reactions Efficacy →	None	Poor	Fair	Good	Excellent
No adverse reactions			X		
Acceptable adverse reactions					
Unacceptable adverse reactions					

Comments, if any: the medication took a long time to act

FIGURE 116

Start of treatment at onset of pain. DENTAL SURGERY FORM A

Diflunisal versus control

To be completed on day of surgery

Name or Initials: F.K.	Age: 22 yrs.	Sex: XX F	Study nr: 87

Procedure: Removal of impacted tooth Impacted element: supernumrary in mandible

Additional surgery, if any: 28

Date of surgery: oct. 5 time 8 a.m. Degree of trauma: mild ☐ moderate ☒ severe ☐

Anesthesia given: general

Exclusion criteria for participation in the study

Please check all items:

	YES	NO
__ Age below legal consent or over 70 years.	☐	☒
__ Confirmed pregnancy or a practical possibility of pregnancy	☐	☒
__ Hypersensitivity to salicylates or to the control medication	☐	☒
__ Current treatment with: systemic corticosteroid or anticoagulants.	☐	☒
__ Active peptic ulcer or g.i. hemorrhage.	☐	☒
__ Significant liver or kidney disease.	☐	☒
__ Hemopoietic disorders.	☐	☒

If none of these conditions applies to the patient, he or she may enter the study and receive test medication + instructions for use.

Start of treatment at onset of pain. DENTAL SURGERY FORM C

Diflunisal versus control

Investigator: Dr M.L. MCCUE

Name or initials: F.K. Study nr: 87

MEDICATION (please record times in 0-24 hours)

Test medication:

first dose was taken at .....hour on day of surgery

second dose was taken at .....hour on day of surgery ☐ */ day after surgery ☐

third dose was taken at ..... - ☐ - ☐

fourth dose was taken at ..... - ☐ - ☐

fifth dose was taken at ..... - ☐ - ☐

If not all doses were used, give reason: no medication required for pain

Did patient take any other analgesic since surgery? No ; Yes

If yes, name of drug: Dose:

Time first dose was taken:

Did patient take strong alcoholic beverages No Yes If yes, specify number of glasses:

Did patient use drugs for other diseases No Yes If yes, specify: (name + dose)

FIGURE 117

DENTAL SURGERY FORM B

Start of treatment at onset of pain.

Diflunisal versus control

Name of investigator: Dr. M.L. MCCUE

Name or initials: F.K. Study nr: 87

CONTROL VISIT Evaluation on of day after surgery date: oct 6 hour: 1300
Only to be filled in if patient took test medication.

1. PATIENTS EVALUATION

Parameters	At intake of first dose of test medication	At control visit	Description of rating scales on opposite page.
1. Pain			
11. Patient's opinion on treatment efficacy			

11. ADVERSE REACTIONS

None, or specify below:	Maximal intensity	Seriousness	Drug relationship	Action taken if any
Adverse reaction codes:	1 = mild 2 = moderate 3 = severe	1=not serious 2=serious	1=definitely not 2=probably not 3=possibly 4=probably 5=definitely	(e.g. dose reduction or discontinuation of test drug)

If adverse reaction was still present at control visit, give outcome if known (mandatory for serious reactions):

completely recovered
residual effects
reaction still present
died

patient receives treatment for reaction: yes; no
if yes, specify:

11. Investigator's overall evaluation taking into account expected spontaneous course of symptoms for individual patient.

Adverse reactions ↓ Efficacy →	None	Poor	Fair	Good	Excellent
No adverse reactions					
Acceptable adverse reactions					
Unacceptable adverse reactions					

Comments, if any: patient required no medication

FIGURE 118

Start of treatment at onset of pain. DENTAL SURGERY FORM A

Diflunisal versus control

To be completed on day of surgery

Name or Initials: I.O.	Age: 25 yrs.	Sex: M / F	Study nr: 88

Procedure: Removal of impacted tooth Impacted element: 38, 48, 45

Additional surgery, if any: 28.

Date of surgery: oct. 7 time: [illegible] Degree of trauma: mild ☐ moderate ☐ severe ☒

Anesthesia given: general

Exclusion criteria for participation in the study

Please check all items:

	YES	NO
__ Age below legal consent or over 70 years.	☐	☒
__ Confirmed pregnancy or a practical possibility of pregnancy	☐	☒
__ Hypersensitivity to salicylates or to the control medication	☐	☒
__ Current treatment with: systemic corticosteroid or anticoagulants.	☐	☒
__ Active peptic ulcer or g.i. hemorrhage.	☐	☒
__ Significant liver or kidney diseases.	☐	☒
__ Hemopoietic disorders.	☐	☒

If none of these conditions applies to the patient, he or she may enter the study and receive test medication + instructions for use.

Start of treatment at onset of pain. DENTAL SURGERY FORM C

Diflunisal versus control

Investigator: Dr. M.L. MCCUE

Name or initials: I.O. Study nr: 88

MEDICATION (please record times in 0-24 hours)

Test medication:

first dose was taken at 1500 ...hour on day of surgery

second dose was taken at 2100 .....hour on day of surgery ☒ / day after surgery ☐

third dose was taken at 0930 - ☐ - ☒

fourth dose was taken at ..... - ☐ - ☐

fifth dose was taken at ..... - ☐ - ☐

If not all doses were used, give reason:

Did patient take any other analgesic since surgery? NO ; Yes

If yes, name of drug: Dose:

Time first dose was taken:

Did patient take strong alcoholic beverages NO Yes If yes, specify number of glasses:

Did patient use drugs for other diseases NO Yes If yes, specify: (name + dose)

FIGURE 119

DENTAL SURGERY FORM B

Start of treatment at onset of pain.

Diflunisal versus control

Name of investigator: Dr. M.L. MCCUE

Name or initials: I.O. Study nr: 88

CONTROL VISIT Evaluation on of day after surgery date: sept. 23 hour: 1100
Only to be filled in if patient took test medication.

1. PATIENTS EVALUATION

Parameters	At intake of first dose of test medication	At control visit	Description of rating scales on opposite page.
1. Pain	3	1	
11. Patient's opinion on treatment efficacy	[illegible]	3	

11. ADVERSE REACTIONS

None, or specify below:	Maximal intensity	Seriousness	Drug relationship	Action taken if any
slight nausea on	1	1	2	none
first dose only				
Adverse reaction codes:	1 = mild 2 = moderate 3 = severe	1=not serious 2=serious	1=definitely not 2=probably not 3=possibly 4=probably 5=definitely	(e.g. dose reduction or discontinuation of test drug)

If adverse reaction was still present at control visit, give outcome if known (mandatory for serious reactions):

completely recovered
residual effects
reaction still present
died

patient receives treatment for reaction: yes; no
if yes, specify:

11. Investigator's overall evaluation taking into account expected spontaneous course of symptoms for individual patient.

Adverse reactions Efficacy →	None	Poor	Fair	Good	Excellent
No adverse reactions					
Acceptable adverse reactions				X	
Unacceptable adverse reactions					

Comments, if any:

FIGURE 120

Start of treatment at onset of pain. DENTAL SURGERY FORM A

Diflunisal versus control

To be completed on day of surgery

Name or Initials: B.L.	Age: 18 yrs.	Sex: M X F	Study nr: 89

Procedure: Removal of impacted tooth Impacted element: 18,28,38,48.

Additional surgery, if any: none

Date of surgery: oct.7 time am. Degree of trauma: mild ☐ moderate XX ☐ severe ☐

Anesthesia given: general

Exclusion criteria for participation in the study

Please check all items:

	YES	NO
__ Age below legal consent or over 70 years.	☐	X ☐
__ Confirmed pregnancy or a practical possibility of pregnancy	☐	X ☐
__ Hypersensitivity to salicylates or to the control medication	☐	XX ☐
__ Current treatment with: systemic corticosteroid or anticoagulants.	☐	X ☐
__ Active peptic ulcer or g.i. hemorrhage.	☐	X ☐
__ Significant liver or kidney disease.	☐	X ☐
__ Hemopoietic disorders.	☐	X ☐

If none of these conditions applies to the patient, he or she may enter the study and receive test medication + instructions for use.

Start of treatment at onset of pain. DENTAL SURGERY FORM C

Diflunisal versus control

Investigator: Dr. M.L. MCCUE

Name or initials: B.L. Study nr: 89

MEDICATION (please record times in 0-24 hours)

Test medication:

first dose was taken at 1900 hour on day of surgery

second dose was taken at 2330 hour on day of surgery X */ day after surgery ☐

third dose was taken at	0700	=	☐	=	X ☐
fourth dose was taken at	.....	=	☐	=	☐
fifth dose was taken at	.....	=	☐	=	☐

If not all doses were used, give reason:

Did patient take any other analgesic since surgery? X No ; Yes .

If yes, name of drug: Dose:

Time first dose was taken:

Did patient take strong alcoholic beverages X No Yes If yes, specify number of glasses:

Did patient use drugs for other diseases X No Yes If yes, specify:

(name + dose)

FIGURE 121

DENTAL SURGERY FORM B

Start of treatment at onset of pain.

Diflunisal versus control

Name of investigator: Dr. M.L. MCCUE

Name or initials: B.L. Study nr: 89

CONTROL VISIT Evaluation on of day after surgery date: oct. 8 hour: 1100
Only to be filled in if patient took test medication.

1. PATIENTS EVALUATION

Parameters	At intake of first dose of test medication	At control visit	Description of rating scales on opposite page.
1. Pain	4	2	
11. Patient's opinion on treatment efficacy	[illegible]	2	

11. ADVERSE REACTIONS

None, or specify below:	Maximal intensity	Seriousness	Drug relationship	Action taken if any
Adverse reaction codes:	1 = mild 2 = moderate 3 = severe	1=not serious 2=serious	1=definitely not 2=probably not 3=possibly 4=probably 5=definitely	(e.g. dose reduction or discontinuation of test drug)

If adverse reaction was still present at control visit, give outcome if known (mandatory for serious reactions):

completely recovered
residual effects
reaction still present
died

patient receives treatment for reaction: yes; no
if yes, specify: _____

11. Investigator's overall evaluation taking into account expected spontaneous course of symptoms for individual patient.

Adverse reactions	Efficacy → None	Poor	Fair	Good	Excellent
No adverse reactions	0			X	
Acceptable adverse reactions					
Unacceptable adverse reactions					

Comments, if any: the first dose was slow in acting but the following doses relieved the pain satisfactorily

FIGURE 122

Start of treatment at onset of pain. DENTAL SURGERY FORM A

Diflunisal versus control

To be completed on day of surgery

Name or Initials: D.H.	Age: 22 yrs.	Sex: M X F	Study nr: 90

Procedure: Removal of impacted tooth Impacted element: 4,8 ; 38.

Additional surgery, if any: 18, 28.

Date of surgery: sept 27 time am Degree of trauma: mild X
moderate ☐
severe ☐

Anesthesia given: general

Exclusion criteria for participation in the study

Please check all items:

	YES	NO
__ Age below legal consent or over 70 years.	☐	X
__ Confirmed pregnancy or a practical possibility of pregnancy	☐	X
__ Hypersensitivity to salicylates or to the control medication	☐	X
__ Current treatment with: systemic corticosteroid or anticoagulants.	☐	X
__ Active peptic ulcer or g.i. hemorrhage.	☐	X
__ Significant liver or kidney disease.	☐	X
__ Hemopoietic disorders.	☐	X

If none of these conditions applies to the patient, he or she may enter the study and receive test medication + instructions for use.

Start of treatment at onset of pain. DENTAL SURGERY FORM C

Diflunisal versus control

Investigator: Dr. M.L. MCCUE

Name or initials: D.H. Study nr: 90

MEDICATION (please record times in 0-24 hours)

Test medication:

first dose was taken at .....hour on day of surgery

second dose was taken at .....hour on day of surgery ☐ */ day after surgery ☐

third dose was taken at ..... = ☐ = ☐

fourth dose was taken at ..... = ☐ = ☐

fifth dose was taken at ..... = ☐ = ☐

If not all doses were used, give reason:

Did patient take any other analgesic since surgery? No ; Yes

If yes, name of drug: Dose:

Time first dose was taken:

Did patient take strong alcoholic beverages No Yes If yes, specify number of glasses:

Did patient use drugs for other diseases No Yes If yes, specify:
(name + dose)

FIGURE 123

DENTAL SURGERY FORM B

Start of treatment at onset of pain.
Diflunisal versus control
Name of investigator: Dr. M.L. MCCUE

Name or initials: D.H. Study nr: 90

CONTROL VISIT Evaluation on of day after surgery date: _____ hour: _____
Only to be filled in if patient took test medication.

1. PATIENTS EVALUATION

Parameters	At intake of first dose of test medication	At control visit	Description of rating scales on opposite page.
1. Pain			
11. Patient's opinion on treatment efficacy			

11. ADVERSE REACTIONS

None, or specify below:	Maximal intensity	Seriousness	Drug relationship	Action taken if any
Adverse reaction codes:	1 = mild 2 = moderate 3 = severe	1=not serious 2=serious	1=definitely not 2=probably not 3=possibly 4=probably 5=definitely	(e.g. dose reduction or discontinuation of test drug)

If adverse reaction was still present at control visit, give outcome if known (mandatory for serious reactions):

completely recovered
residual effects
reaction still present
died

patient receives treatment for reaction: yes; no
if yes, specify: _____

11. Investigator's overall evaluation taking into account expected spontaneous course of symptoms for individual patient.

Adverse reactions ↓ Efficacy →	None	Poor	Fair	Good	Excellent
No adverse reactions					
Acceptable adverse reactions					
Unacceptable adverse reactions					

Comments, if any: could not contact the patient

FIGURE 124